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THE JOURNAL *of* The Maine Medical Association

VOLUME 61 JANUARY 1970 NUMBER 1

Research in Maine Number

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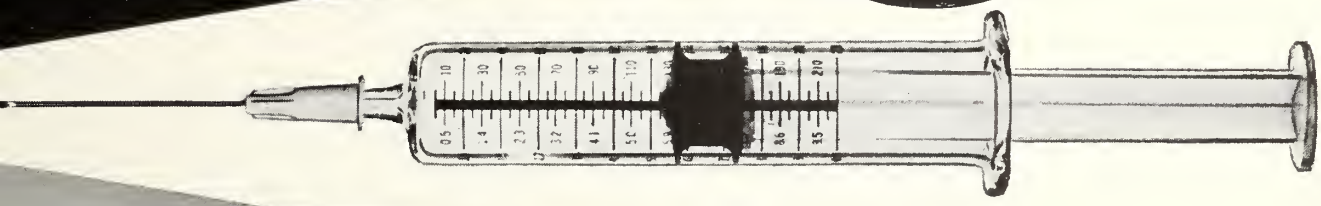

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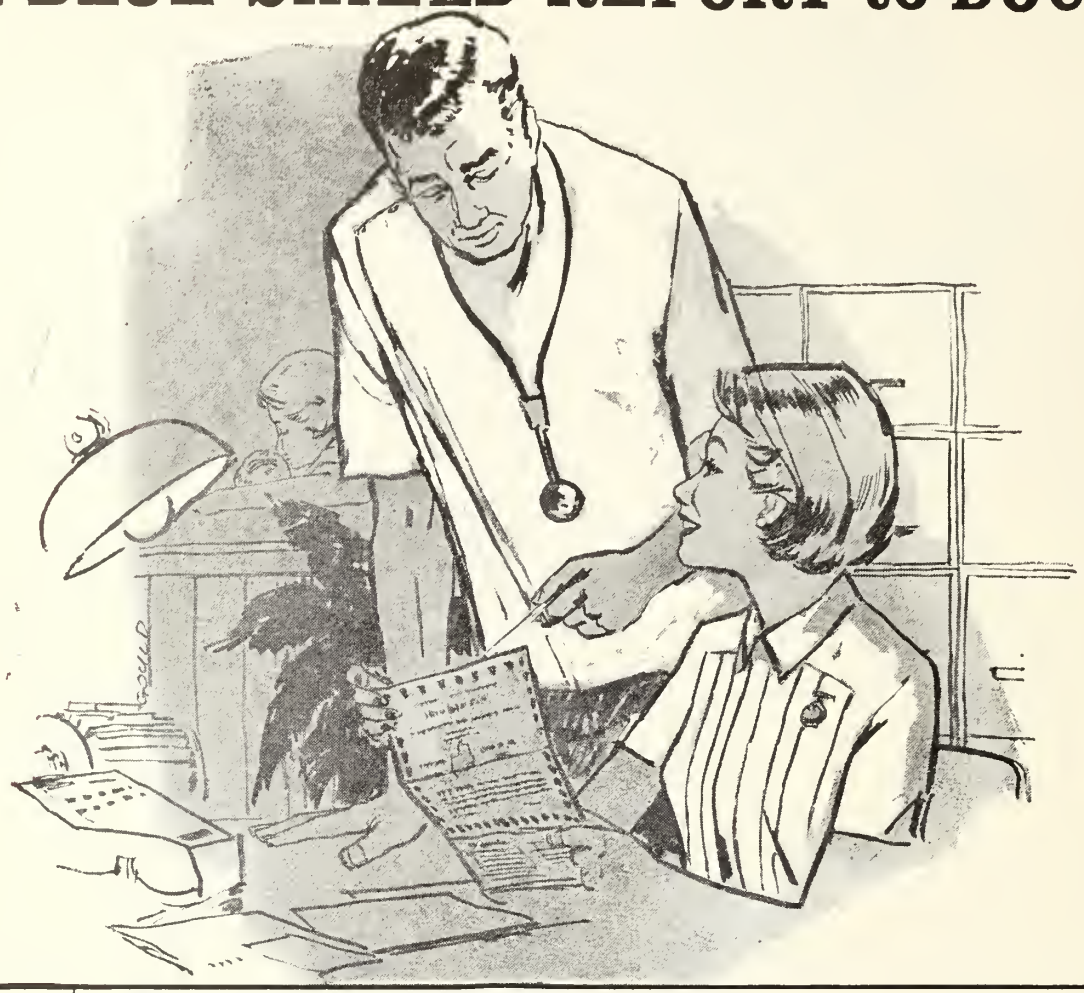

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The Journal of the Maine Medical Association

Volume Sixty-one | Brunswick, Maine, January 1970 | Number 1

Research in Maine

The status of research in Maine, as well as the rest of the country, has been a confusing issue to the physician, the granting institution, and the researcher. Recently, some factors relating to the position of research relevant to granting institutions and public funds were put forth by Dr. Jay P. Sanford in his presidential address before the National Meeting of the American Federation for Clinical Research. Because his comments are appropriate and the information contained in them is not likely to be easily available to the practicing physician, it seemed appropriate to publish his comments with the permission of the Editorial Board of the Journal of Clinical Research. The following is the text of his speech and I believe it serves as its own commentary.

Has Clinical Research Failed in its Public Trust?*

JAY P. SANFORD, M.D.**

Has clinical research failed in meeting the trust placed upon it by the American Public? Have the American taxpayers, who have been footing this ever-increasing bill, been getting their money's worth or has Congress been giving away the taxpayer's dough to the eggheads? In this day of rapid and almost instant communication, of unequaled crowding, of enormous economic pressures, of minimal requirements for physical labor and hence maximum free time, of unbridled materialism and of constant, organized "protesting" – whether right or wrong – it is easy to become stampeded and to attempt to cure the symptoms before the cause has been elucidated. The temptation to succumb at times to expediency and faintheartedness is understandable. Today there is a growing sense that we in clinical investigation may have been building a Tower of Babel for personal aggrandizement or escape rather than pursuing our ultimate objectives, the conquest of disease, and the assurance of health for all of our citizens-that is, a state of complete physical, mental and social well-being not merely the absence of disease or infirmity.

In 1948, Congress increased the budget of the National Institutes of Health from 8 to 28 million dollars, enabling the pattern of the NIH to be molded.[2] Then in June of 1956, Congress essentially doubled the appropriations for the National Institutes of Health and thereby inaugurated the era of growth in medical research.[2,3] By this action, Congress in effect established that it would be national policy to try to conquer disease and insure health through research, no matter how long or difficult the task. As tax-supported research funding approached the billion dollar mark, the support of science inevitably became a major issue of public policy. In the last 20 years, 10,000,000,000 dollars of Federal money have been invested in the implementation of this policy.[4]

In June of 1966, at the launching of Medicare, President Johnson expressed concern that insufficient attention was being given to the application of the results of laboratory health sciences research to the health problems of our nation.[5] This concern has been articulated into at least four major charges. First, basic research has not contributed significantly to the establishment of health or to the management of disease. Second, the majority of biomedical investigators have withdrawn themselves from the arena of application or development of basic knowledge to the solution of health problems. Third, there exists a "significant body of fundamental information which is stagnantly awaiting application by competent practitioners."[6] Fourth, clinical faculty members are devoting too much of their energies and time to research, at the expense of teaching and the delivery

*Presidential Address presented before the National Meeting at the American Federation for Clinical Research, Atlantic City, New Jersey, May 4, 1969.

**Professor of Medicine, the University of Texas Southwestern Medical School at Dallas, Texas.

of health care. As a corollary, there has been a changing emphasis in clinical investigation from patient-centered, disease-oriented research toward non-human, non-disease oriented research.[7]

As clinical investigators, each of us must examine these allegations not from the standpoint of self-interest but from the vantage of what have been the accomplishments and what should be the goals and future approaches of biomedical research. From conclusions based upon analysis of these data, we must be prepared and willing to alleviate our deficiencies and to promote our strengths to the broad medical community, the American public and Congress.

First, has basic research contributed to the establishment of health or to the management of disease? My answer, unequivocally, is yes! Yet, since 1955, a time which roughly correlates with major availability of funds for biomedical research, the general death rate in the United States stopped its long downward trend and has fluctuated over a narrow range, 9.2 to 9.4 per 1000 population, depending largely on the presence or absence of major influenza outbreaks.[8] Certainly, these data would not appear to support the value of our research effort. Unfortunately, as was well developed in the analysis by Williams, there has been an overemphasis on life-saving as the primary goal of biomedical research and care programs.[4] This emphasis was most clear in the report of the President's Commission on Heart Disease, Cancer and Stroke.[9] The dividends from basic research can be better illustrated by individual examples. The area of infectious and communicable diseases provides some of the more striking examples. The polio and measles vaccine sagas are now so well accepted that we tend to forget them as recent advances. The current example, live attenuated rubella virus vaccine, well illustrates the value of basic research. The demonstration of viral interference, certainly a non-human, non-patient centered, non-disease oriented observation if viewed in vacuo, enabled Parkman and associates and Weller and Neva to devise a system and isolate rubella virus in 1961.[10,11] The subsequent attenuation, development and testing of vaccines affords the promise of control of rubella with a degree of effectiveness comparable to that for measles.[12] During the last major rubella epidemic in 1963-1964, there were an estimated 20,000 children born with birth defects including cataracts, glaucoma, cardiac defects, mental deficiency and deafness. The annual cost for providing care and education is approximately 9,000 to 13,000 dollars per child. Dr. Louis Cooper, Director of the rubella birth defect evaluation center at Bellevue Hospital Center, estimates that the dollar burden on the public, without consideration of suffering and potential loss of income, following the 1963-1964 epidemic will be 2.8 billion dollars.[13] Other examples of the value of basic research which might be mentioned would include the study of soil ecology, the isolation and taxonomy of streptomycetes, which led to the treatment of tuberculosis and other infections with streptomycin; or the development of electrophoretic analysis of plasma proteins, a basic research technique which provided one of the bases for definition of the immunoglobulins. These observations proceeded to the demonstration of secretory IgA, an understanding of which has now led to the real possibility of developing more effective means of immunizing against respiratory disease agents such as influenza which, as I have pointed out, do reflect in mortality statistics. As Dr. Weinberg of the Oak Ridge National Laboratories stated at the conference "Research in the Service of Man," "The bulk of biomedical science is in the prefeasibility stage and therefore the underlying basic research must be done broadly."[14] If research is to conquer disease, it must stick to the central tack of acquiring basic knowledge.

The second general allegation relates to the lack of application of the available scientific knowledge toward the provision of health. It must be recognized that the full application of basic knowledge encounters many obstacles. For example, the medical case against smoking as one potential factor in carcinoma of the lung or chronic airways disease, the latter now being second only to heart disease as a cause of adult disability, is very strong. The same failure of implementation would hold in the area of highway safety and seat belts. Yet, broad segments of the public not only condone but have actively blocked attempts to implement these health measures. It equally well might be charged that clinical investigators all too frequently have been responsible for the premature extension of research procedures into clinical practice under circumstances whereby the public fails to grasp the investigative nature of the procedure. Although the recent implantation of a mechanical heart has excited the imagination of the public, its justification even as an investigative procedure is controversial. As Dr. Bennett testified before the Harris Subcommittee on Government Research, in 1967, "A paucity of basic knowledge is often the greatest impediment to a program of development."[15]

There is much current debate about our investment in basic research, versus applied or mission oriented research, versus the provision of health services. If one only looks at dollars, the total cost of health care to the nation is 55 to 60 billion dollars. "The portion devoted to medical research is only about 2.5 billion dollars, or 5 percent, and the Federal share of this is about two thirds or 1.6 billion dollars. Thus, it is clear that even a billion dollars shifted to the health service bill, although ruinous to medical research and education, would contribute little to the service problems."[16] The upcoming cutbacks in research training grants and fellowships at the moment the nation faces an urgent and growing need not only for more physicians but also for more medical faculty members would seem to epitomize false economy.[17] The report of the Gottschalk Committee illustrates that even the solution of a biochemical problem which ideally seems suited to solution through the

application of available knowledge, chronic renal insufficiency, poses serious problems.[18] Hemodialysis which is life-saving carries the attendant hazard of infection, hemorrhage and thrombosis, not to mention the huge economic burden. The present economic burden is about 10,000 dollars per patient per year, and it is estimated that as many of 5,000 patients each year reach the stage of being logical candidates for a dialysis program. Thus, the cost might approximate 50,000,000 dollars per year. The need to define the cause glomerulonephritis, to determine factors concerned with its progression and hopefully with such information, to prevent or modify the course of disease is apparent. The situation is analogous to the relationship between iron lungs and virus research in poliomyelitis as existed in 1950; both are important, but an either-or position is myopic.

Third, as to the question of a communications gap, if failures occur, it is largely because the best minds knowledgeable in the field fail to conceive or understand the possible relations of the new knowledge to utility. From an analysis of the abstracts submitted to the three clinical societies during 1953 to 1965, Feinstein and associates demonstrated a progressive decrease in the proportion of abstracts from human, patient-centered, disease-oriented categories toward those categorized as non-human, non-disease oriented.[7] They concluded: "We have not attempted to judge the causes or values of the trends"; however, the implication pervades their presentation that this was contrary to the best interests of clinical investigation. Yet, as one reviews the abstracts presented at the Annual Meetings of the American Federation for Clinical Research since 1944 and places them in the perspective of time, it seems apparent that many of the seemingly clinically irrelevant papers have formed important steps in the structure of our current clinical practice. Certainly, the argument that each abstract has or will have clinical relevance cannot be supported; however, the proportion which does have clinical relevance is sufficient to strongly support the view that the Atlantic City meetings afford an excellent means to facilitate the incorporation of new knowledge into the solution of clinical problems.

Fourth, briefly, the plea most recently voiced by Doctor Castle that "the faculty should strive to make all their teaching efforts more relevant to the prevention, understanding and treatment of disease" cannot be disputed.[19] The question is one of defining that body of information which is relevant – Is messenger RNA or the role of cyclic AMP as a transmitter of hormonal messages relevant? J. Robert Oppenheimer put the matter well: "It is proper to the role of a scientist that he not merely find new truth and communicate it to his fellows, but that he teach, that he try to bring the most honest and intelligible account of new knowledge to all who will try to learn. It is one reason why the patronage of science by and through universities is its most proper form, for it is here in teaching and association of scholars . . . that the narrowness of scientific life can best be moderated and the harmonies of scientific discovery can find their way into the wider life of men."[20]

Clinical research today has not achieved all that has been expected of it, in part as a consequence of unrealistic goals in the mind of the American public, in part because of social pressures and in part because the task is incredibly complex. As clinical investigators, we must not be mindless of these deficiencies, yet we do not have to hang our heads and apologize for our handling of the public trust toward reaching our goal-the provision of health and the conquest of disease. Finally, if we succeed in maintaining public and Congressional confidence in our goal, we must continually remind ourselves that the future is not merely an extension of the present.

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Continued on Page 6

The pH of Intravenous Solutions

Some Chemical Considerations*

WILLIAM H. AUSTIN, M.D. and VALERIE V. FERRANTE, M.T. (ASCP)

Recently, there have been a number of papers and several letters dealing with acidity of intravenous solutions.[1-12] The production of thrombophlebitis by dextrose and water has been reported and various suggestions have been made concerning alkalinization in an attempt to overcome this difficulty. It is not generally agreed, however, that the pH per se is the cause of phlebitis[1,13] and results differ from study to study. If phlebitis is produced by acidosis or by other means, it does not appear to be a serious problem.

The titration of dextrose and water or saline used in intravenous solutions produces the expected response (Fig. 1). Both solutions are initially slightly acid and can be easily further acidified or alkalinized by the addition of very small amounts of acid or alkali. These intravenous solutions are poor buffers in the physiologic range and hence their pH is dictated to a large extent by the media into which they are introduced. Others containing the salts of weak acids such as acetate, gluconate and lactate show a mixed type of response when titrated. For example, when Normosol®-R,† (pH 6.12) or Normosol®-R-7.4,* (pH 7.29) is titrated from its

*Supported by a grant from the Maine Heart Association.
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†Abbott Laboratories, North Chicago, Illinois.

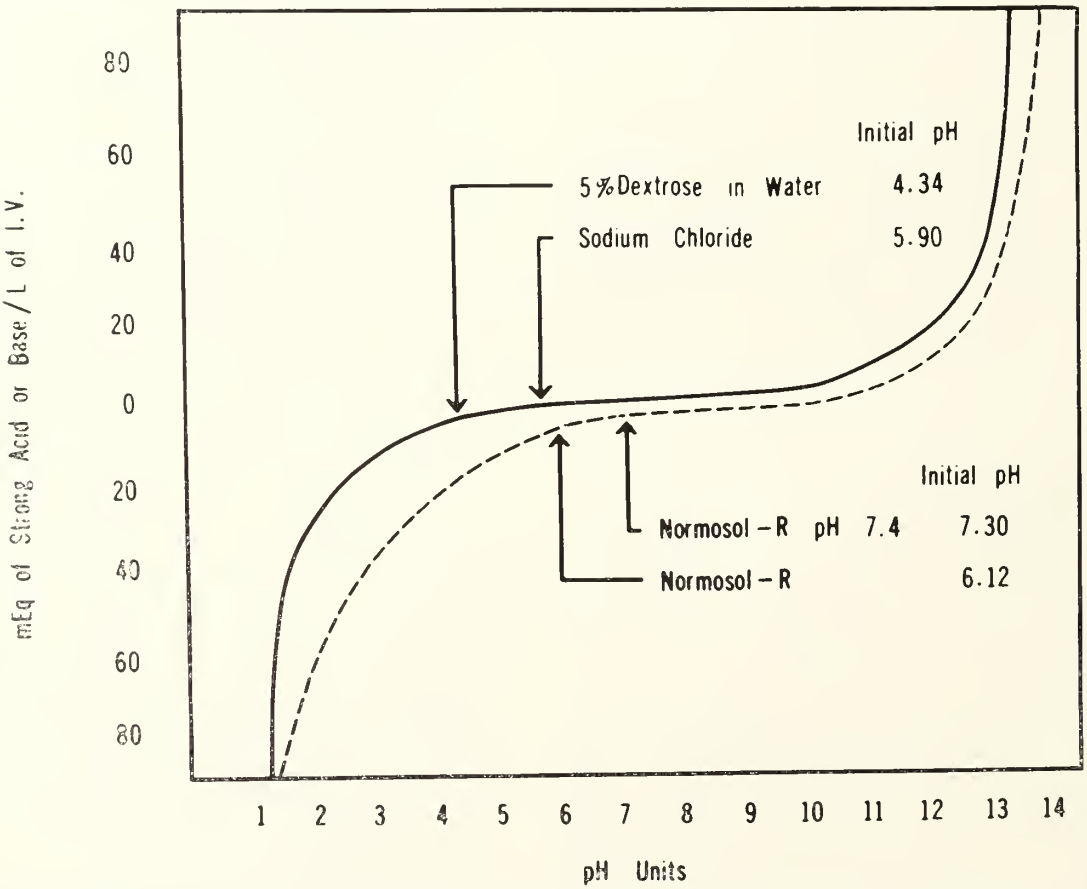

Fig. 1. Titration curves of various intravenous solutions showing initial pH with the zero point expanded for visual purposes. Although not strictly accurate, 5% D/W and isotonic saline are depicted as a single curve for ease of presentation. Even though it is not apparent because of the scope of the diagram, 0.84 mEq of strong base is required to raise the pH of each liter of Normosol-R to 7.3; 0.02 mEq to raise the pH of sodium chloride, and 0.05 mEq for 5% dextrose in water.

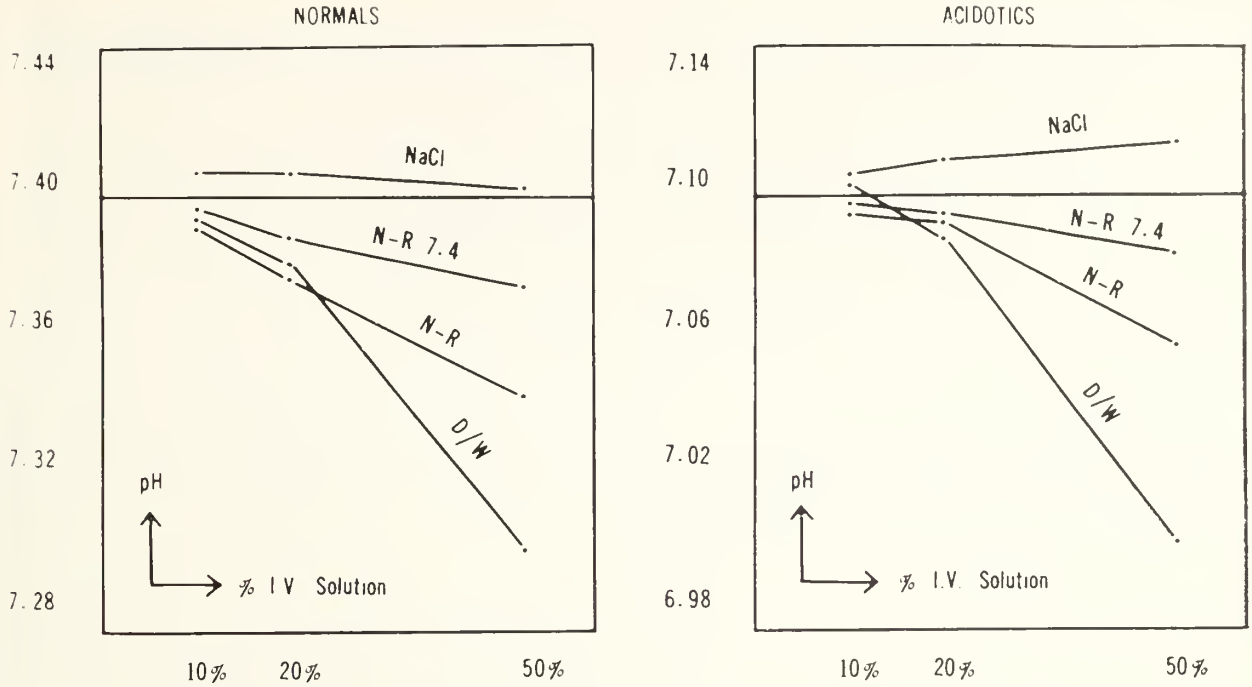

Fig. 2. A graphic representation of the mean changes in pH in 8 normal and 8 acidotic samples of whole blood after adding various amounts of intravenous solutions: Sodium Chloride (NaCl), Dextrose and Water (D/W), Normosol-R-7.4 (N-R 7.4), and Normosol-R (N-R).

existing pH with a strong acid, a flatter curve results which is characteristic of the salt of a weak acid. The pK', judging from the titration curve (Fig. 1), is in the vicinity of pH 3 at approximately 25°. When alkali is added, the response is much like that seen with saline. It is apparent that the difference in the two balanced solutions, one pH adjusted, the other not, is extremely small and can be obliterated by a minute quantity of acid or base.[14] The important fact to emphasize is that the so-called balanced solutions (i.e. non-bicarbonate containing mixtures) do not behave like buffers in the physiologic range and justification for their use cannot be a greater pH stabilizing effect in the immediate post infusion period.

Addition of various solutions to blood gives some indication of the effect of I.V. solutions on the ultimate pH of the mixture. To achieve this, various anaerobic combinations of blood and I.V. solution were made (Fig. 2). It should be realized that this is not comparable to *in vivo* administration of intravenous solutions since whole body buffering would further diminish the acidifying effect of an I.V. solution. However, it can be seen that mixing blood with 5% dextrose and water, isotonic saline, buffered or unbuffered balance solution produces little change in the pH (Fig. 2). Dextrose and water may produce a slightly lower pH than saline; however, for practical purposes, the differences are insignificant. What is significant is that even though during fluid administration acute local changes might result, the ultimate pH is similar to that of the blood. This indicates what has long been maintained, that the blood is a very good buffer. Acetate, lactate and gluconate salts are eventually converted to bicarbonate; however, the immediate effect of the administration of balanced solutions, regardless of their pH, is not unlike that seen when saline is given.

Although we are unable to comment on the possibility of thrombophlebitis resulting from an acid solution, it seems unlikely that any systemic effect from large intravenous fluid administration could occur. It also appears that the so-called balanced solutions, even those whose pH's have been adjusted, offer no immediate advantage except possibly in the replacement of alkali deficits.

However, as previously noted[15] when the prevention or correction of metabolic acidosis is in order, bicarbonate, rather than the salt of some other weak acid, seems to be the agent of choice.

This communiqué is not intended to discredit solutions which contain the salts of weak acids. Rather it is to point out that a significant immediate stabilization of pH is not achieved through the use of one of these mixtures. It is further contended that such solutions as dextrose and water or saline, although acid, are quickly and easily neutralized by blood and extracellular buffered mechanisms.

Addendum

Since the preparation of this manuscript, it has come to our attention that at least one manufacturer has marketed a neutralizing additive ($NaHCO_3$) for intra-

venous use. In view of the results of our report and the cost of this material, the use of such an additive seems unwarranted except in special situations. If it can be demonstrated that a given material is more stable at a neutral pH or that the incidence of phlebitis can be reduced by an additive, we would favor its use. At present, there is no good information to support either contention.

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Assignment Method of Payment Under Medicare

If the patient and physician agree to the assignment method of payment, Medicare reimburses the physician directly. Under this method the physician agrees to accept the charge determination of the Carrier as the **full** charge. Therefore, the patient should **not** be billed for any reductions in charges made by Medicare. The patient, of course, is still responsible for any amounts applied toward the $50 deductible and the 20% not covered by Medicare.

Conversely, if a physician does not agree to the assignment method, Medicare reimburses the patient. Under this method, the patient is responsible for the full charge made by the physician. — **From Medicare Health Insurance Part B, Box 4629, Portland, Maine.**

Biological and Medical Research in Maine: a Survey

PETER W. RAND, M.D.*

Acting on the premise that health-related research within the state could contribute broadly to improved patient care, and, therefore, that a mechanism should exist to attract funds for its support and growth, the Maine Medical Association at its annual meeting in June, 1968 established a Research Fund Committee. In presenting his resolution for the appointment of this committee, its architect, Dr. Saul R. Polisner of Portland, emphasized the present critical need for this type of financing not only to provide new programs throughout the state but also to check the erosion which had already affected Maine research as a result of Federal cutbacks.

As its first goal, the Research Fund Committee† chose to gather information concerning a) the present magnitude of biomedical research in Maine, b) attitudes regarding the role of hospital-based research, and c) local or statewide problems relating to human health which might be solved through applied research. To accomplish this, questionnaires were sent to each of the state's 70 hospitals, to all institutions of higher learning offering science courses, and to independent research facilities. The findings of this survey are reported in this paper.

We must stress at the outset that deficiencies both in the content and distribution of our questionnaires as well as in the response of a few addressees limit specific interpretation of the results in some areas. On the other hand, through the generous cooperation of most respondents this survey provides for physicians and researchers alike a detailed summary of the direction and scope of biological and medical research in the state, some idea of the feelings of the medical community toward research, and an enlightening list of priorities for future investigation.

THE SURVEY

Two sets of questionnaires were sent: the first to the directors of all allopathic and osteopathic hospitals as listed in the Directory of Maine Hospitals and Schools of Nursing,[1] and the second to the presidents of Maine's colleges, to the chairmen of each science-oriented department in the University of Maine, and to the directors of the Jackson Laboratory, the Mount Desert Island Biological Laboratory, the Bureau of Commercial Fisheries Laboratory, and the Biological Laboratory of the Maine Department of Sea and Shore Fisheries. The hospital questionnaire, accompanied by a return-addressed, stamped envelope, was mailed in the early spring of 1969; second and third mailings were made to non-responders through September. Only one mailing, in July, 1969, was made to the academic and research institutions. The contents of these questionnaires appears below:

HOSPITAL QUESTIONNAIRE

1. Is research being conducted at your institution? If *yes,*
   a. List the names and departments of your investigators, the title of their projects, an estimate of their annual budget and its source, and their recent publications.
   b. What is your total annual research budget?
   c. How much space is allotted to the research laboratories, offices, etc.?
   d. What is the size and composition of your research staff?
   e. What services, other than academic output (consultations, educational programs, tests, reagents), does your facility provide?
   f. Do you have definite plans for expansion within the next five years?
2. (for institutions with no research programs)
   a. Do you feel that research has a place in Maine medicine?
   b. If *yes,* do you feel that it should be centralized in larger institutions, or should it be promoted generally?
   c. Is the establishment of research programs at your hospital within the next five years definitely planned, probable or improbable?
3. (for all respondents) Please list any problems peculiar to your locality (epidemiological, environmental, etc.) which might be solved through applied research.
4. (for all) Please list individuals who might be interested in the development of, or participation in, biomedical research in Maine.
5. Please use the space below for any remarks or recommendations you might have.

ACADEMIC INSTITUTION-RESEARCH FACILITY QUESTIONNAIRE

1. What is the size of your research staff? (specify number of investigators, assistants, technicians, etc.)
2. What is the approximate size (sq. ft.) and apportionment of your research space?
3. For each current or planned research project please list the title, principal investigator, budget, supporting agency, and provide, if possible, a list of pertinent publications.
4. Please list major facilities and equipment related to biological and medical research.
5. Suggest others who might be interested in contributing information to this survey.

RESULTS

1. Hospital Questionnaire

Sixty-one of Maine's 70 hospitals (87%) replied to our questionnaires. Of these, 10 indicated on-going research projects (see Table 1). To encourage as much

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†Original Membership: Saul R. Polisner, M.D., Benjamin Zolov, M.D., Stanley G. Dienst, M.D., Mason Trowbridge, M.D., Advisor: Peter W. Rand, M.D.

participation as possible, respondents were not provided with preconceived definitions of "biomedical research" or "research funds." As a result, their replies reflected a wide spectrum of interest and activity ranging from progressive health-care delivery projects to highly specialized and sophisticated laboratory investigations. Despite the severe limitations placed on research by clinical practice, many physicians who had the opportunity to participate in the survey (and, to our knowledge, many who did not) reserved a meaningful part of their time for clinical research work.

Six hospitals reported specifically funded laboratory research, and at least two indicated separate research departments staffed by full-time investigators. Although complete lists of publications were not submitted in all instances, the volume and quality of contributions, particularly from institutions housing full-time research, was substantial.

While innovative programs of health-care delivery may not fit the traditional image of clinical investigation, they are, in a very real sense, research in a field which, as underscored by responses to the third part of our hospital questionnaire, is vital to the interests of Maine physicians and their patients. Although only two hospitals classified programs in this area as research, we have, in recognition of this interest, obtained a listing of currently funded projects of Maine's Regional Medical Program, which are presented below.

MAINE'S REGIONAL MEDICAL PROGRAM:
APPROVED OPERATIONAL PROJECTS
(The Funding Shown Is For a 15 Month Period Ending 9/30/70)

Visiting Guest Resident Project $36,391

Objectives: To continue and expand a program initiated by the Bingham Associates Fund which sends senior residents or fellows at Tufts-New England Medical Center to small community hospitals. This establishes a line of communications between the University Hospital Center and the relatively isolated practioners.

Kennebec Valley Regional Health Agency Program $241,745 (offices in Waterville)

Objectives This project establishes cooperation between Maine's Regional Medical Program and the Regional Health Agency of Maine's Upper Kennebec Valley in the development of a regional approach to comprehensive health care and planning for rural area residents.

Smoking Control $48,626 Approximately 300 sq. ft. in Augusta

Objectives: This project is designed to improve the health status of Maine people through an educational and action program directed against "cigarette disease." Basic work has already been done by the Maine Interagency Council on Smoking and the Health Council of Maine. This project involves Maine's Regional Medical Program in these activities and provides a coordinator and other staff assistance, office equipment and supplies, and administrative funds.

Coronary Care Program $198,462 Located in Maine Medical Center

Objectives: This is a comprehensive program designed to bring the latest advances in diagnosis and treatment to patients with acute coronary disease by establishing coronary care units in 20 community hospitals over a five-year period. These hospitals will be linked by remote monitoring methods to referral centers where expert consultation services are available on a 24-hour basis. Included in this program are: 1) planning consultation service; 2) training programs for nurses; 3) training programs for physicians; 4) visiting physician program; 5) paramedical consultation service; 6) operational aids, data collection, and evaluation; 7) hospital cardiopulmonary resuscitation programs; 8) possible mobile coronary care units (future); and, 9) remote monitoring by communications media.

Physicians' Continuing Education Program $76,285

Objectives: This project will establish teaching programs in 20 community hospitals and five groups of small community hospitals. Four programs will be presented annually to the staffs of these hospitals in the areas of heart disease, cancer, stroke and rehabilitation.

Core Program $578,807

Objectives: The major objectives of the administrative shift from planning to core will be to connect operational projects to the planning process. Other goals are: 1) provide leadership and assistance in the development and accomplishment of program objectives: 2) maintain regional relevance within individual operational projects; 3) update and re-define operational objectives; and 4) expand the services of the Research and Evaluation Unit at the University of Maine.

Director of Medical Education Program* $27,122 being implemented for one year with carry over funds)
To be based at Augusta General Hospital for 4 hospitals.

Objectives: Proposes a "third faculty" composed of Directors of Medical Education. Expanded and improved opportunities for continuing education of rural area health professionals is the major emphasis of this program.

Regional Library* $42,828 (being implemented for one year with carry over funds)
Based at Maine Medical Center – approximately 100 sq. ft. of space.

Objectives: Expand the existing facilities of the Maine Medical Center Medical Library so that it can more adequately function as a regional medical library.

Problem-Oriented Medical Records $61,163 – 2,000 sq. ft. Augusta General Hospital
(Approved Contract Project Under Medical Care Development, Inc.)

Objectives: 1. To design and test a training effort based on the use or problem-oriented medical needs in an ambulatory care setting.
   a. Including curriculum design, trainee selection criteria, educational content analysis, use of teaching aids, etc. as appropriate.
2. To train physicians and paramedical personnel from Maine and other regional medical programs in the use of POMR in ambulatory care.
3. To measure the short-term and long-term effects of the training program on the behavior of the trainees. Various educational components such as barriers to physician learning, objective measures of behavior, attitude formations, retention of knowledge, attainment of skills, and changes over time (at least a twelve month follow-up) will be evaluated.

Some indication of the diversity and magnitude of hospital research in Maine is provided by totaling the data from the first part of the questionnaire. Within the ten reporting institutions at least 40 professionals, 14 of whom indicate full-time research commitments, are en-

*Approved but not funded.

TABLE 1: Data From Responses to Part I of Hospital Questionnaire

Institution	Investigator	Project Area	Annual Budget	Source of Support	Publications	Research Space	Total Staff	Services	Expansion Plans
Bangor State Hospital	Magaro	Schizophrenia	30,000	U.M. Bur. MH&C	1		Pl 4 GS/F 15		
	Turner & Magaro	remotivation in psychotics				lab. 3000 off. 2400	A/T 1 S 1 N,O 7 28	educational programs	yes
Dudley Coe Infirmary Bowdoin College	Hanley	orthopedic athletic injuries	0	-	0	0	Pl 1 N 1 A/T 1 S 1 4	consultations	no
Eastern Maine Medical Center	Clason	resuscitative medicine	17,100	MHA	-	-	-	education, communication, training	-
	Lopez & Madaras	laboratory methodology	29,769	1	-		Pl 1 A/T 4	education	yes
	Trowbridge	pernicious anemia detection	-	-	pending	lab. 950 off. 800	S 1 6	B-12, folic acid uropepsin determination	yes
Maine Coast Memorial Hospital	Lambdin	delivery and medical care	-	P	3	-	Pl 7-8 GS/F 1	consultations educational programs	yes
	Stadler	rural medical profile	-	RMP PP	0	-	A/T 2 10-11		
Maine Medical Center	Austin	acid-base chemistry and electrolyte metabolism	21,000	MHA FFS I	14/8 yrs.				
	Johnston	role of hormones in arthritis, aldosterone immunoassay, effect of estrogen antibodies on estrogen dependent tumors, prostoglandin physiology	48,000	MHA PTAF FFS 1	3/2 yrs.				
	Nelson	factors in vector-cardiographic analysis	45,000	NIH AHA	36/8 yrs.	lab. 1900 off 850 lib. 350 an. qtr. 3000 shop 250	Pl 5 A/T 11 S 3 19	consultations educational programs, special diagnostic tests, reagents	yes
	Rand	hemorhcology, microcirculation, oxygen delivery	40,000	NIH MHA PF 1	14/8 yrs.				
	Ritchie	automated immunoassays, diagnostic role of specific plasma proteins, antinuclear antibodies, computer applications to above.	57,000	PTAF MHA PF FFS I	11/4 yrs.				
	these & other members of staff	other research projects			72/8 yrs.				
Millinocket Community Hospital	Desjardin	blackfly bites	-	PP	0	0	Pl 1	-	-
Pineland Hospital and Training Center	Apaydin	effect of phenothiazines on EEG	-	1	pending	-			
	Hoffman	adjustment of discharged retardates	21,000	HEW	3	-			
	Kimura	INH toxicity	-	1	-	-			
	Pelletier	auditory thresholds in retarded (planned)	-	1	-	-	Pl 1 A/T 2 S 1 4	genetic counciling special tests	No
	Staff	infantile autism	-	1	-	-			
	Rerrick	sex chromatin anomalies; mucopolysaccharidosis; homocystinuria	-	1	4, others pending				
	Other members of staff				89 papers, films, and presentations since 1959				
Thayer Hospital	Goodof	lipids in relation to atherosclerosis	0	-	-	-	GS/F 1 A/T 1 2	-	-
Veterans Administration Hospital	Brum	metabolism of glyoxal							
	Dana	atherosclerosis							
	Emanuel	sphincter function							
	Fongemie	prenatal visual stimulation							
	Malcom	alcoholic personality							
	Metcalf	transplant immunology							
	Ohler	delerium tremens treatment evaluation							
	Paquette	effects of histamine on gastric lipase	93,000	VA	6 12 presentations	lab. 2516 off. 764 lib. 168 an. qtr. 162	Pl 4 A/T 1 S 2 7	assistance with clinical studies, educational programs, consultations, statistical evaluations.	No
	Paris	temporary dental fillings							
	Rothstein	psychosocial personality model							
	Sanders	programmed learning							
	Smith	endocrine morphology							
	Sobel	ox-facia hererotransplants							
	Spellman	I^{131} on gastric secretions							
	Turner	sulphur cpds on rat gastric ulcer							
	Whiteside	programmed learning in dietetic service							
Webber Hospital	Osher Edgar Anton LaFond Viger	feasibility of coronary care unit in a community hospital without full-time cardiologist	5,000	RMP MHA	pending	CICU 400	Pl 5 N 6	electronic communication and consultation.	Yes

KEY:
- AHA - American Heart Association
- Bur. MH&C - Bureau of Mental Health & Correction
- FFS - Fees for Services
- HEW - Department of Health, Education, & Welfare
- I - Institutional Budget
- MHA - Maine Heart Association
- NIH - National Institutes of Health
- PF - Private Foundation
- PP - Private Practice
- RMP - Maine's Regional Medical Program
- PTAF - Pine Tree Chapter, Arthritis Foundation
- VA - Veterans Administration

Staff:
- Pl - Investigators
- GS/F - Graduate Students, Fellows
- A/T - Assistants, technicians
- S - Secretary
- N - Nurse
- O - Other

gaged in basic biochemical, physiological and biophysical investigation in a wide variety of medical, psychiatric, and surgical studies, and in a number of health-care delivery projects which are broad both geographically and in respect to their approach. Because much of the money for this effort has been absorbed in institutional budgets, has not been reported, has been approximated, or refers to varying periods of time, the true annual investment in hospital research in Maine cannot be identified by adding up the figures in Table 1. Recognizing that similar limitations apply to research space assessments, it can only be estimated that 8500 sq. ft. of research laboratories, 4800 sq. ft. of offices, and 3000 sq. ft. of animal quarters exist in the state. Although the volume of published material gives some index of academic output, this survey unfortunately provided no yardstick by which the educational, consultative, diagnostic and other service by-products could be measured. Their value will become more tangible as hospital research expands.

The second part of the questionnaire examined the attitudes of non-research hospitals toward clinical research in Maine. Of the 51 institutions responding to this part, 47 (92%) felt that research had a place in Maine medicine, one felt unqualified to express an opinion, and three (6%) saw no place for research here. Two of the last group made no further comment, while the third felt that the need for improved medical standards and health care delivery took exclusive precedence over the desirability of research.

Asked to chose the location of clinical research, 28 (62%) of the 47 who approved its existence favored centralization in larger institutions, 17 (36%) felt it should be encouraged in all hospitals, and 2 had no opinion. Seven of the 51 respondents who did not have research in their hospitals felt that they would have within five years, 40 did not think so, and 4 were uncertain.

The third question, regarding local health problems which might be solved through applied research, was answered on 21 (34%) of the 61 returned questionnaires. The 35 individual items mentioned are categorized and identified by county in Table 2.

Fifteen individuals (25%) responded to the final request for remarks or recommendations: five of these re-emphasized their feelings about the need for improved health-care delivery, four described potential research or innovative clinical programs within their own institutions, three discussed the relative merits of the location of research, one stressed the need for continuing medical education, and two registered general support for medical research.

2. Academic Institution – Research Facility Questionnaire

Replies were received from 11 of 24 colleges canvassed, from 7 of 25 science departments at the Orono and Portland campuses of the University of Maine, and from each of 4 independent research laboratories. Since programs which truly relate to biological and medical research do not exist in many of the institutions and departments queried, the fact that all questionnaires were not returned does not necessarily indicate inadequate sampling. Indeed, with one or two exceptions, it would appear that the majority of academic units which provide this type of research have responded. The independent research laboratories all contributed voluminously; we regret being unable to include more of this significant material in the report.

In Maine's institutions of higher learning, at least 55 investigators are researching (one third of them on a full-time basis) and publishing in scientific disciplines which relate in varying degrees to life and health. Although the size of their technical staff is, in general, not large, many programs are augmented by graduate student participation. In most, but not all instances, sufficient space for research is available or is under construction. Equipment inventories at the University of Maine and at Bowdoin College include such sophisticated items as computers, electron microscopes and ultracentrifuges, in addition to the usual assortment of analytical instruments. Several institutions have marine collecting facilities; Nasson College lists a mobile biology laboratory.

Most research projects in these institutions depend heavily on individual grants for their support: a wide variety of federal, state, industrial and private sources is represented. It is indeed unfortunate that our survey did not include a question relating to changes in the level of research support during the last few years, and to the effects of any such changes on research programs and productivity. As with the hospital questionnaire, it is difficult to estimate from the information provided how much money is used specifically for biologically or medically oriented research in Maine's academic institutions each year. The amount would appear to exceed $500,000.

The independent research facilities sent questionnaires to the Jackson Laboratory, the Mount Desert Island Biological Laboratory, and the Biological Laboratories of the U.S. Bureau of Commercial Fisheries and the Maine Department of Sea and Shore Fisheries. Although the work of the latter two facilities is less directly related to human physiology, the analytical techniques and equipment employed are in many instances similar to those used in medical research and thus comprise an important segment of the resources for biomedical research in the state. Selection of these four laboratories was made on an arbitrary basis; failure to include in the survey any other independent research effort in the state was not intentional. We did elect, however, not to extend the study at this time to industrial research programs. Information regarding this sector has recently been compiled.[2]

The Jackson Laboratory is the largest and most productive biomedical research institution in Maine. It enjoys well-deserved international renown as a leader in

TABLE II: LOCAL PROBLEMS NEEDING APPLIED RESEARCH

Category	*Items Listed*	*County*
Environmental Pollution	water pollution: parathione poisoning	Aroostook
(8 respondents)	bronchitis-emphysema in potato-house workers	Aroostook
	air and water pollution	Piscataquis
	ENT infections in lake swimmers	Cumberland
	air and water pollution	Cumberland
	lake pollution	Somerset
	air pollution from sulfite paper mills	Penobscot
Health Care Delivery (6 respondents)	application of modern medicine to community hospital practice	Hancock
	utilization of available medical services	Washington
	delivery of area health services	Cumberland
	the specialist as a generalist	Penobscot
	use of medical assistants in rural health care delivery	Hancock
	teaching of rural medicine to students and house officers	Hancock
Specific Medical Problems (13 respondents)	occupation medicine; leukemia	Penobscot
	ski and skimobile accidents	Kennebec
	mechanism of sports injury, URI's; densensitization procedures	Cumberland
	hereditary diseases in coastal communities	Hancock
	population genetics; erysipeloid rural geriatrics	Aroostook
	cancer therapy, thyroid metabolism, chronic renal disease, coronary angiography and surgery	Androscoggin
	tuberculosis control	Somerset
	is blastomycosis endemic?	Aroostook
	allergy and chronic sinusitis	Knox
	obesity in pregnancy	Penobscot

genetics research and as a supplier of highly inbred strains of mice to research laboratories world-wide. Members of its scientific staff exhibit the highest degree of competence and achievement in their disciplines and hold important positions in professional activities here and overseas. During the 1968-'69 fiscal year,[3] 26 investigators conducted 57 research projects, almost all with inbred strains of mice, which related to neoplasia, hematology, metabolic disorders, reproduction, behavior, and allied subjects. Sixty-nine students were enrolled in four research training programs, ten post-doctoral fellows were in residence, collaborative projects were carried out with 30 visiting investigators, 90 people attended a two-week course in genetics, 39 seminars were held, and 79 papers were published by members of the staff. Project support, which totaled $2,184,000, was derived

TABLE III: Information Supplied by Respondents to Academic Institution - Research Faculty Questionnaire

AAS = American Academy of Science
ACS = American Cancer Society
AEC = Atomic Energy Commission
DA = Department of the Army
I = Institutional Grant
MDAA = Muscular Dystrophy Association of America
NASA = National Aeronautical & Space Administration
NIH = National Institutes of Health
NSF = National Science Foundation
PF = Private Foundations
PRF = Petroleum Research Fund
USDI = U.S. Department of the Interior

Institution or Department (Respondent)	Research Staff (PT = part time): Professional Investigators	Assistants, Fellows	Graduate Students	Technicians	Secretaries	Others	Research Space (square feet): Laboratories	Offices	Conference Rooms	Animal Quarters	Library	Other	Current Research Projects: Principal Investigator	Title of Project	Financial Support and Source	Publications	Facilities and Equipment
BOWDOIN COLLEGE Biology Department (Dr. Gustafson)	3 PT	0	3-4 honors students	1 1 PT	-	-	2200	Available		300	Available		Howland Moulton Knoulton	Oxidative biochemistry Pine structure of teleost ear; Directional hearing in fish; Study of neurones Marine plankton	30,000 NIH, NSF 5,000 NSF, PF, I 1,000 NSF, PF, I	many including book several pending	Electron microscope, IBM 1620 computer, low temperature incubators, histological equipment, high speed centribuges, preparative ultra-centrifuge, spectrophotometers (Zeiss, Perkin-Elmer, Durrum, Aminco-Change), cold room, marine station with boat and collecting gear, etc.
Chemistry Department (Dr. Mayo)	6 1 PT	1 5 PT	0	I 3 PT	1	1	3000	1500	300	100	600	2000	Hyams Mathis Mayo Settlemire Sheats Wheatland	Vibration spectra: heavy metals Biochemistry of algae Ramin spectral studies of natural products Membrane ion transport mechanism Synthesis of metallogenes Synthesis of chelation agents	20,000 USAF 2,500 PRP 5,000 AAS, NFS, NIH, PF 2,500 PRF 4,000 NSF, PF 2,000 PRF	11 22 3 4	Gas chromatographs; visible, UV, IR spectro-photometers, K-band spectrometer, nuclear magnetic resonance spectrometer.
Division of Science and Mathematics (Dr. Fitzgerald)	6 PT	-	-	6 PT	-	-	400	Science building with extensive facilities to be completed 9/70.					Johnston	Pilot project in water pollution studies for York County	-	-	Visible UV and IR spectrophotometers, chromatography and electrophoresis equipment, mobile biology laboratory, Warburg apparatus, polarograph, etc.
RICKER COLLEGE (Dr. Schark)	-	-	-	-	-	-	-	-	-	-	-	-	Schark	Sulphonium compounds (extracurricular project)	-	-	Microscopes, chromatographic equipment, spectrophotometer.
SOUTHERN MAINE VOCATIONAL TECHNICAL INSTITUTE Department of Applied Marine	2	-	4 PT	-	1	-	216	687	636	538				Applied marine biology and oceanography Hydrographic survey of Casco Bay	80,000 NSF I	1 -	3 research vessels, several boats, oceanographic collecting and analyzing apparatus, hydrographic equipment, aquaria, microscopes, histological apparatus.
UNIVERSITY OF MAINE (ORONO) Department of Biochemistry (Dr. Radke)	5 PT	2 PT	4 PT	1 PT	1 PT	-	1000	400	avail-able	600	avail-able	-	Radke DeHass Lerner Hancock Wratten	Nutrition, esp. proteins Enxymology and nutrition Amino acid absorption Nucleoproteins Enzyme kinetics	88,060 past 2 yrs. NASA, NSF, State	12 6 7 - 3	Extensive, not specifically listed.
Department of Geological Sciences (Dr. Osberg)	7 PT	-	6 PT	-	1	-	1260	1920	0	0	0	2200	Norton	Distribution and dispersal of arsenic in pleistocene aquifers in southeastern Maine	40,000/2 yrs. NIH, USDI	-	X-ray defractometer, atomic absorption unit.
Department of Zoology (Dr. Allen)	14 PT	1	42	2	3	2	22000	2200	600	3380	avail-able	2000	Cook, Dean, Dearborn, Dolphin, Hatch, Haynes, McAlice, McCleave, Major, Myer, Munn, Roberts, Speicher, Valleau	36 biological research projects with emphasis on marine organisms	327,000 in project grants for periods up to 5 years. Faculty research grants - F.Y. '68-'69 approx. $168,000 NASA,NIH, NSF,PF, and other Federal, State sources	22 during F.Y. 1968-1969	Electronmicroscope, X-ray unit, physiographs, Coulter counter, spectrophotometers, microscopes, boat, skiffs, collecting gear, radiation detection equipment, aquaria.
Department of Food Science (Dr. Hogan)	4	5	1	-	1	-	2200	400	a v a i l a b l e			1800	Hogan Highland Murphy Illyn	Food quality and safety (potatoes, shrimp, poultry, fruit, vegetables)	100,000 Federal, State, Industry	not listed	Thin layer, paper and gas chromatographic equipment; microbiological and chemical equipment; pilot food processing plant.
Darling Oceanographic Center (Dr. Myers)	6	2	2	3	2	5	3000	2 rooms		-	-	-	Dean, Blake, DeWitt, Fink, McAlice	19 studies in marine biology, hydrography, geology	95,310 State, Federal, Private Industry	not listed	Research vessel, 3 boats, oceanographic collecting and analyzing gear, photomicroscopic equipment, computer, etc.
THE JACKSON LABORATORY (Dr. Green)	26	277	11	14	30	30	14683	8695	1404	38265	1527	54532	Bailey, Bernstein, Bronson, Chai, Cherry, Coleman, Collins, Dickie, Eleftherio, Fowler, Fox, Fuller, Green, Griffen, Hancock, Hummel, Hutton, Kalias, Kandutch, Les, Meier, Murphy, Myers, Roderick, Russell, Sawin, Schlager, Snell, Stevens, Waymouth, Whitten, Werboth, Wimer, Yuhas	57 projects in the field of radiation, aging, reproduction, teratology, heredity, development, regulation, metabolism, behavior, animal health, husbandry, and research training	2,184,100 F.Y. '68-'69 ACS, AEC, DA, MDAA, NIH, NSF, PF	79 F.Y. '68-'69 9 books and 2 symposia/10 yrs.	Art, photography and replicating services, biochemistry equipment, laboratory computing service, electron microscope, histotechnical service, library, X-ray.
MOUNT DESERT ISLAND BIOLOGICAL LABORATORY (Dr. Wilde)	32	18	9	not listed			8 laboratory buildings, shop and stockroom, office and library, meeting hall, dormitory, cottages. dock.						Adamson, Boylan, Burg, Crawford, Cserr, Doyle, Epstein, Fenstermacher, Forster, Goldstein, Grant Hogben, Huang, Janicki, Kinter, Kleinzeller, Maren, Murdaugh, Opdyke, Peirce, Rall, Rappaport, Rhodin, Rieck, Schmidt-Nielsen, Settles, Smith, Wilde.	45 projects in various areas of physiology and biochemistry with emphasis on marine vertebrates (lab. operates June, July and August only).	59,434 NSF, PF, dues, fees, investment income	publications not listed 37 reports and 14 seminars during '69 season	Collecting boat and skiff, marine biological collecting gear, fresh and salt water aquaria, microscopes, centrifuges, ultracentrifuges, Warburg apparatus, flow photometer, pH meter, isotope counters, etc
BUREAU OF COMMERCIAL FISHERIES Biological Laboratory (Dr. Skud)	18	5 PT	1 PT	10 9 PT	4	10	15,000 total space						Graham, Sherman, Welch Ridgeway, Stickney, Cooper Skud, Anthony Uzmann Boyar, Watson Kensler	Basic oceanography Immunogenetics of marine animals Ecology and behavior of marine animals Population dynamics of marine animals Parasitology of marine animals Life history of marine animals Aquaculture	600,000 U.S.D.I.	326 over 26 years	2 research vessels, 15 boats and skiffs, oceanographic collecting and analyzing equipment; electrophoretic, histological, chemical and microscopic equipment, environmental monitors.
DEPARTMENT OF SEA & SHORE FISHERIES (Dr. Dow)	16	3	-	9 5 PT	5	-	6400 present total space; 8000+ additional space planned						Apollonio, Baird, Creaser, Dow, Flagg, Goggins, Harriman, Hurst, Reed, Richards, Ricker, Rinaldo, Sterl, Thomas, Varney, Wallace	30 projects related to fisheries research	690,000 State, Federal, Private Industry	221 over 17 years	2 research vessels, 15 boats and skiffs, oceanographic collecting and analyzing equipment, histological equipment gas chromatography, microscopic equipment.

entirely from grants awarded to investigators from a wide variety of Federal and private agencies. The laboratory houses all basic equipment for the projects being conducted plus some specialized items, including a recently-installed electron microscope.

The Mount Desert Island Biological Laboratory, located at Salisbury Cove, is apparently the oldest biological research facility in Maine, having been founded at South Harpswell in 1898 and moved to its present location in 1921.[4] It operates only during the summer months. Many years of physiologic research of the highest calibre performed on marine organisms by scientists from many fields, including medicine, have contributed to this laboratory's excellent reputation. In 1969, its scientific staff of 59 included 32 investigators, one postdoctoral fellow, nine graduate students and 17 assistants. These individuals were divided into 28 research groups which carried out 45 projects related to renal physiology, electrolyte transport, respiration and circulation, to mention a few areas. The operations of the laboratory are financed primarily by fees charged for the use of the facilities, grants from the National Science Foundation, and private donations. The physical plant consists of 13 buildings containing basic research equipment, a dock, collecting boat and skiffs.

The U.S. Bureau of Commercial Fisheries Biological Laboratories at McKown Point, West Boothbay Harbor, has been in operation since 1905. Its mission has been exclusively marine biological research since 1948. The facility consists of eight buildings housing several laboratories, a large and comprehensive library and reprint collection, and residences. The laboratory has a large dock, two research vessels (65 and 40 feet), collecting gear and basic research instrumentation. Over the last twenty years the staff has averaged fifteen published papers annually, most of which have dealt with fisheries resources, population dynamics and ecological factors. The laboratory's annual budget of $600,000 is funded through the U.S. Department of the Interior.

The Marine Research Division of the Maine Department of Sea and Shore Fisheries, with offices in Augusta and laboratories also on McKown Point in West Boothbay Harbor, has carried out broad and extensive research programs related to all aspects of marine biology and fisheries resources along the coast and in the tidal estuaries of Maine. Mutual cooperation is enjoyed with the neighboring Federal facilities in Boothbay. Although part of their laboratory building was destroyed by fire two years ago, a present construction program will almost triple their original research space. Equipment includes two research vessels (63′ and 42′), 15 small boats, extensive oceanographic gear and laboratory instrumentation. An annual budget of $690,000 is provided by appropriations, license fees, industry taxes, Federal matching funds and industry grants. During the last year, 16 researchers have conducted 30 projects, several of which were in the currently important areas of pollution and aquaculture. While the ecology and management of each of Maine's commercially valuable species has received emphasis in the 221 papers published by the members of the staff over the last 17 years, the laboratory's bibliography in general represents an encyclopedia of Maine coast biology.

A recent addition to the field of research in Maine is the Research Institute of the Gulf of Maine (TRIGOM). This organization, which has its central offices in the Science Building of the University of Maine in Portland, represents a cooperative effort by eight member academic institutions in southern Maine to coordinate and conduct marine research. A 2400 square foot laboratory, which will contain flowing sea water aquaria and appropriate scientific instruments, is under construction on the campus of Southern Maine Vocational-Technical Institute. A project to investigate the effects of sublethal concentrations of petrochemicals and emulsifiers, to be carried out with the collaboration of the Research Department of the Maine Medical Center, is being planned.

Discussion

Although a recent comprehensive study has been made of the state's marine research efforts,[5] and an earlier compilation of its industrial research programs is available,[2] we have found only one current reference related to medical research.[6] While this Federal survey did not include information about facilities or projects, it did present some pertinent facts regarding the size of Maine's health-related research effort in 1968. It placed the combined areas of floor space devoted to this pursuit at 103,000 sq. ft., and the total expenditure, from all sources, at $2,818,000. These figures represented, respectively, only 0.25% and 0.22% of the national totals. In spite of the few proud examples of established research and the several promising programs of new research which appear in our survey, only half as much health-oriented investigation is being carried out in Maine, on a per capita basis, as elsewhere in the United States.

The compelling need for expansion of all research in Maine, if only to help meet the state's rapidly multiplying problems in the area of human ecology, cannot be denied. While the tools and talents for this growth can only be supplied through increased financial commitments from both governmental and private sectors, continuing search should be made for methods to increase the productivity and application of Maine research. It is apparent from the facts gathered here that separation, in both distance and purpose, is characteristic of the distribution of research facilities in the state. As a first step toward increasing research efficiency, serious consideration should be given to the improvement of communication and collaboration between laboratories.

But the medical profession itself, in expressing its awareness, if not anxiety, concerning the efficiency of health care delivery, has provided the most forceful argument for the establishment, throughout Maine, of

clinical research programs. Much of this issue relates to the system of delivery, but an important segment involves the availability of up-to-date medical knowledge to the practicing physician. Investigators, attracted to Maine by the presence of clinical research, can supply this knowledge. Since it is both the raw material for their work, and the product which brings them support, their presence makes it available to their practicing colleagues at a minimum of expense to the patient and the community. Its only requirement for efficient operation is that the investigator be allowed to maintain his academic productivity, without which grants cannot be won in these fiercely competitive times. If medical research is thus recognized and encouraged as a distinct system, as a separate approach to the attainment of improved patient care, a symbiotic relationship between clinical and academic medicine in Maine will be created, which, while benefitting both partners, will also benefit the patient.

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22 Bramhall St., Portland, Maine 04102.

AMA Judicial Council: Billing for Treatment of Family Member

The Judicial Council of the American Medical Association recently issued the following statement regarding the provision of medical care to members of a physician's family: "From time immemorial it has been considered unwise and improper for a physician to treat members of his immediate family for other than minor health problems or in emergencies. For him to do so would be in violation of Section 6 of the Principles of Medical Ethics and therefore unethical.

"Even if for some good reason it becomes necessary to treat a member of his immediate family, a physician should not charge, or make a claim for, or receive compensation for such service from the patient or from a third party payor on the patient's behalf." — **News Release from the A.M.A., No. 34, Nov. 1969.**

Practical Diagnostic Endocrinology for the Non-Endocrinologist

PHILIP G. WHITNEY, M.D.

Extensive recent advances in the medical subspecialties have made it increasingly difficult for the practitioner of general medicine to keep abreast of current developments in areas of medicine in which he is not continually involved. This brief review is written for those practitioners who do not maintain a day to day contact with problems related directly to endocrinology but who are confronted with possible glandular disorders frequently enough to utilize a good screening approach. An attempt will be made to outline currently acceptable procedures.

Great strides in laboratory technology over the last two decades have led the way to better understanding of the pathophysiology of glandular disorders and have also made available to the "rural" practitioner the tools to confirm many of the common endocrinopathies seen in general medicine. These tools, or laboratory techniques, are now available in several Maine hospitals and within 24 hours of any location in the State through several Boston laboratories. Emphasis has been away from cumbersome and frequently inaccurate 24-hr. urine collection techniques and toward tests on single and multiple blood specimens. With clinical suspicion as his most important weapon, the diagnostician is now able to include or exclude a number of common endocrinopathies in out patients with more than fair reliability.

THYROID

Excluding diabetes, disorders of the thyroid are undoubtedly the most frequent of the glandular disorders. Four categories of thyroid function tests exist for general use:

A. *Thyroidal iodine uptake,* available as radioactive iodine uptake (RAIU).

B. *Peripheral blood iodine,* available either as protein bound iodine (PBI), protein bound butanol extractable iodine (BEI) or T4 iodine by column, a measure of thyroxine iodine after thyroxine is separated from other iodoproteins.[1]

C. *Peripheral blood thyroxine* as total thyroxine (T4) by I-125 assay,[2] now available in several Maine hospitals, or free thyroxine by radioimmunoassay (not available except as a research tool). It should be noted that the "T4 test" may mean any of three available tests: T4 by column, total thyroxine by I-125 binding displacement, or free thyroxine by radioimmunoassay. The method of T4 measurement must be known to determine the significance of the result.

D. *Thyroid Binding Protein Saturation* as T3 uptake. A measure of unused binding sites on thyroid binding proteins and thus an indirect measure of peripheral thyroxine. This test, the T4 by I-125 assay and the RAIU require radioisotope techniques.

Functional abnormalities of the thyroid gland presenting as either hyperthyroidism or hypothyroidism can be more reliably confirmed with the use of one test from two of the above four categories. These tests are influenced by many variables including contamination with iodides, drug effect and more recently the wide spread use of oral contraceptives. Group A or uptake testing is uneffected by estrogens and most drugs but is depressed by iodine contamination or increased by iodine deficiency. Group B tests are contaminated by iodides and elevated by estrogens. Group C and D tests are uneffected by iodides but influenced by estrogens as well as many other drugs. In patients with suspected hyperthyroidism, a T4 by I-125 and a T3 uptake will uncover hidden iodide contamination and suggest hidden drug effect or estrogen effect, for only if both tests are elevated can one support a clinical suspicion. Elevation of T4 and depression of T3 suggests estrogen effect. Depression of T4 and elevation of T3 suggests androgen or Dilantin® effect.

Hypothyroidism is best screened by a T4 by I-125 and an RAIU or group B test. If doubt exists after standard testing, a TSH (thyroid-stimulating hormone) stimulation test is frequently helpful. In this test, a 5 cc. I.M. injection of Thyrotrophin is given after an RAI and 24 hours later a second RAI is obtained. Patients with primary hypothyroidism show little or no increase in uptake where as patients with normal glands will almost always show uptakes above 25%. Three days of TSH stimulation is entirely unnecessary except in the situation in which one is attempting to separate primary from secondary myxedema.[4]

In the face of both iodine contamination and estrogen influence, one still may use the BMR as a confirmatory test. Factors effecting the reliability of the BMR are well known and when considered make this a worthwhile test. Values of minus 15 to plus five are considered in the normal range. It should be stressed that the measure of ankle reflex time is not a reliable measure of hyperthyroidism.[3] Its use should be restricted to screening for hypothyroidism and in titrating thyroid therapy in hypothyroidism.

Given a patient with borderline tests for hyperthyroidism and a diffusely enlarged gland, a suppression test is sometimes helpful. Following an RAIU, the pa-

tient is given 75 mgs. of Cytomel® q.d. for seven days followed by a repeat uptake. Failure of suppression of uptake by greater than 50% strongly suggests an abnormal gland which if not already producing toxicity may do so in the future.

The antithyroid antibody study may show elevation in a variety of thyroid disorders but is highly positive in Hashimoto's auto-immune thyroiditis. It should be noted that this test is occasionally elevated in auto-immune disorders without thyroid involvement clinically.

The clinical use of LATS (long acting thyroid stimulator) analysis in patients with Graves disease is still experimental. The assay, which is a bioassay, is positive in only about 60% of cases making it a poor screening test even if it were readily available. Many endocrinologists believe that LATS is etiological in Graves disease. This gamma globulin is an antithyroid antibody which attacks the follicle cell microsome and seems in some way to "turn it on" to increasing activity. Unfortunately, this gamma globulin has been found in high concentration in patients who are not clinically hyperthyroid but who have exophthalmus and pretibial myxedema, again suggesting it's worthlessness in screening the hyperthyroid patient.

Parathyroid

Although numerous sophisticated tests of calcium excretion and phosphate reabsorption have at times been very much in vogue, the repeated measurement of serum calcium remains the best and most reliable test of parathyroid function.[5] Hypercalcemia is reliably measured on the auto analyzer and its persistence suggests hyperparathyroidism until proven otherwise. Radioimmunoassay of parathormone is still experimental but is now judged to be a reliable research tool and should be available to the practitioner within several years, finally opening the door to the secretive parathyroid adenoma which may be behind many a renal stone and duodenal ulcer.

Hypoparathyroidism remains a rare disorder which is often difficult to diagnose. The repeated measure of serum calcium and PO4 and the use of the Ellsworth-Howard test still remain the best laboratory tools. Careful evaluation of renal and GI function is necessary in all hypocalcemic patients since chronic renal disease and malabsorption disorders are more often causes of hypocalcemia. All serum calcium aberration must be evaluated in the light of serum proteins since increase or decrease in serum protein levels will produce increase or decrease in total serum calcium.

Adrenal Cortex

The separation of the patient with Cushings Syndrome from the patient with obesity, adult onset diabetes and hypertension has until recently been a time consuming and expensive process. Now this distinction can be reliably made with the out patient Decadron® suppression test.[6] The patient is given 1 mg. of Decadron by mouth at 11:00 P.M. the evening before an 8:00 A.M. plasma cortisol. Values of 8 ug.% or less for plasma cortisol are considered normal and virtually rule out Cushings Syndrome. Values above 8 ug.% should be further investigated with in hospital urine collections before and during a standard oral Decadron suppression test in which Decadron is given at 0.5 mg. doses every 6 hours for 8 doses. In normals, urine on day two should contain less than 50% of baseline urinary hydrocortisone. Further separation of causes of Cushings Syndrome will not be detailed but can be found in all standard endocrinology texts.

Tests of adrenal cortical insufficiency are best made in the hospital with the intravenous ACTH test. Patients who are truly suspected of having adrenal insufficiency should be given maintenance Decadron in doses of 0.5 mg. b.i.d. or t.i.d. Forty units of ACTH in 1000cc 5% D&W is given over a period from 8:00 A.M. to 4:00 P.M., and urine collection beginning at 8:00 A.M. is completed 24 hours later. Normal adrenal glands should produce 25 mgs. hydrocortisone in the second 24 hours of stimulation. Patients with adrenocorticol insufficiency rarely are able to increase levels of hydrocortisone above baseline and values under 10 are highly suggestive of insufficiency. Plasma cortisol levels during the 6th hour of stimulation should be more than double the baseline level. This measure may be used in place of urine collection if difficulty in urine collection is experienced.

It should be pointed out that patients with adrenal insufficiency frequently have completely normal baseline urinary steroids and that the ACTH stimulation test is all important in substantiating the diagnosis. It should also be noted that hydrocortisone is the measurement of importance and that urinary 17 ketosteroids should not be relied upon for diagnosis.

Cortical tumors producing aldosterone induced hypertension should be sought in middle aged females with hypertension and hypokalemia (all due respects to Dr. Conn).[7] If urinary aldosterone is elevated and plasma renin is depressed (especially if measured after the patient has been up and about for four hours),[8] the patient should be referred to a center where selective adrenal vein catheterization and adrenal venography can be done. Melby and Kahn in Boston are also measuring adrenal vein angiotensin levels to help the surgeon select the correct adrenal to attack.

Adrenal Medulla

Screening for pheochromocytoma is now satisfactorily done with urinary VMA levels. Regitine and histamine tests may be helpful in highly suspected cases but should not be used routinely. Either test may be dangerous in the presence of an actual pheochromocytoma.

Testes

For diagnostic purposes male hypogonadism may be conveniently divided into hypogonadotrophic hypogona-

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It is the time when motivation is highest—when a new mother needs expert advice for the future, so she can space her children and limit her family.

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Non-nursing mothers may begin Ovulen-21 immediately after delivery, on the day of departure from the hospital or at the first postpartum visit, as desired. It is recommended that nursing mothers begin Ovulen-21 four weeks after delivery.

A small fraction of the hormonal agents in oral contraceptive pills has been identified in the milk of mothers receiving these drugs. The long-range effect on the nursing infant cannot be determined at this time.

Indication—Oral contraception.

Contraindications—Thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia, undiagnosed abnormal genital bleeding.

Warnings—Watch for the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism, retinal thrombosis); if present or suspected discontinue the drug immediately.

British studies reported in April 1968[1,2] estimate there is a seven- to tenfold increase in mortality and morbidity due to thromboembolic diseases in women taking oral contraceptives. In these controlled retrospective studies, involving 36 reported deaths and 58 hospitalizations due to "idiopathic" thromboembolism, statistical evaluation indicated that the differences observed between users and non-users were highly significant. The conclusions reached in the studies are summarized in the table below:

Comparison of Mortality and Hospitalization Rates Due to Thromboembolic Disease in Users and Non-Users of Oral Contraceptives in Britain.

Category	Mortality Rates		Hospitalization Rates (Morbidity)
	Age 20-34	Age 35-44	Age 20-44
Users of Oral Contraceptives	1.5/100,000	3.9/100,000	47/100,000
Non-Users	0.2/100,000	0.5/100,000	5/100,000

No comparable studies are yet available in the United States. The British data, especially as they indicate the magnitude of the increased risk to the individual patient, cannot be applied directly to women in other countries in which the incidences of spontaneously occurring thromboembolic disease may differ.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or sudden onset of proptosis, diplopia or migraine. Withdraw medication if papilledema or retinal vascular lesions are found.

Since the safety of Ovulen in pregnancy has not been demonstrated, it is recommended that pregnancy be ruled out for any patient who has missed two consecutive periods before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the first missed period.

A small fraction of the hormone agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect on the nursing infant cannot be determined at this time.

Precautions—Pretreatment physical examination should include special reference to the breasts and pelvic organs, and a Papanicolaou smear.

Endocrine and possibly liver function tests may be affected by Ovulen. Therefore, it is recommended that such tests if abnormal be repeated after the drug has been withdrawn for two months.

Pre-existing uterine fibromyomas may increase in size under the influence of progestogen-estrogen preparations.

Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation.

In breakthrough bleeding, and all irregular vaginal bleeding, consider nonfunctional causes. Adequate diagnostic measures are indicated in undiagnosed vaginal bleeding.

Carefully observe patients with a history of psychic depression and discontinue the drug if severe depression recurs.

Any possible influence of prolonged Ovulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study.

A decrease in glucose tolerance has occurred in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be observed carefully while receiving Ovulen.

Because of the effects of estrogens on epiphyseal closure Ovulen should be used judiciously in young patients in whom bone growth is not complete.

The age of the patient constitutes no absolute limiting factor, although Ovulen therapy may mask the onset of the climacteric.

The pathologist should be informed of Ovulen therapy when relevant specimens are submitted.

Adverse Reactions—A statistically significant association has been shown between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: cerebrovascular accidents, neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement, secretion), change in weight, changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, allergic rash, rise in blood pressure in susceptible individuals, mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme and nodosum, hemorrhagic eruption, itching. The following laboratory results may be altered by oral contraceptives: hepatic function: increased sulfobromophthalein and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test; pregnanediol determination.

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Contraindications: Hypersensitivity to antihistamines. Not recommended for use during pregnancy.
Precautions: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension.
Side Effects: Hypersensitivity reactions including skin rashes, urticaria, hypotension and thrombocytopenia, have been reported on rare occasions. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered.
Dosage: 1 Extentab morning and evening.
Supplied: Bottles of 100 and 500.

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dism, in which urinary levels of FSH are low, and hypergonadotrophic hypogonadism, in which urinary levels of FSH are normal or high. FSH bioassay is accomplished in several Maine hospitals and offers a very gross quantitation of pituitary gonadotrophins. (Urinary FSH by bioassay measures both FSH and LH). Urinary and plasma testosterone have recently become available and offer more definitive measures of testicular function. These analyses are available through New England Nuclear Biomedical Laboratories with good reliability although they are still quite expensive. Male patients with suspected hypogonadism should have assay of urinary or plasma testosterone. If this bears out the clinical suspicion, FSH bioassay levels will suggest whether the disease is localized to the testicle or the pituitary. If testicular disease is suspect, testicular biopsy is usually necessary for diagnosis. If pituitary disease is suspect, IM chorionic gonadotrophin can be given as 5000 I.U. per day for three days with repeat measure of plasma or urinary testosterone. Elevation of plasma testosterone above 0.25 mg.% confirms the diagnosis of hypogonadotrophism and localizes the disease to the pituitary. Recently, very sensitive measures of FSH and LH have been developed by radioimmunoassay. These methods are not as yet available to the practitioner.

Ovary

Discreet glandular causes of hirsutism, secondary amenorrhea, and infertility are the exception rather than the rule but none the less must be sought. If history and general physical examination do not uncover an obvious cause, screening evaluation of these disorders should include at the very least a careful pelvic examination and urinary 17 ketosteroids and 17 hydroxysteroids.

Large polycystic ovaries and normal urinary steroids make a sclerocystic syndrome or Stein Leventhal syndrome a likely diagnosis. Patients with this disorder frequently have elevated urinary and plasma testosterone (testosterone is not a 17 ketosteroid) but rarely have elevated ketosteroid values. Wedge resection of the ovaries not only facilitates ovulation but appears to correct the ovarian steroid dysgenesis in such a manner that patients frequently return to normal in all respects.

Elevated levels of urinary ketosteroids suggest an adrenal etiology. Suppression tests are indicated in this situation. If ketosteroid levels are reduced to below 5 mg.% after three days of Decadron 0.5 mg. every 6 hrs., one has strong evidence against Cushings disease due to adrenal adenoma or carcinoma and suggestive evidence for the relatively common benign androgenic adrenal hyperplasia.

It is then necessary to determine whether the patient's condition warrants long term adrenal suppression with Prednisone® or analogs of cortisone. Sclerocystic syndrome may still be present in latent form arising as a result of abnormal adrenal steroidogenesis. Finally, both ovarian and adrenal aberrations may be secondary to sustained noncyclic FSH output. This situation can be managed with cyclic estrogen therapy usually without simultaneous steroid suppression. The mechanism of sclerocystic syndrome and its relation to hypothalmic-pituitary adrenal disease is still incompletely understood and therapy remains somewhat empirical.

Pituitary

Good methods of quantitating anterior pituitary function are still not readily available to the Maine physician. Although serum levels of growth hormone, ACTH, FSH and LH are now measurable by radioimmunoassay, these tests are still experimental and have not been adopted by commercial labs. on a local level. Very indirect and certainly less reliable methods of accessing pituitary function include the Metyrapone test and urinary FSH levels by bioassay.

The Metyrapone test requires a normal adrenal gland as demonstrated by intravenous ACTH tests. Metyrapone blocks cortisol synthesis thus decreasing the normal shut off mechanism to ACTH secretion. Under Metyrapone influence, increased anterior pituitary ACTH stimulates the adrenal to put out precursors of cortisol in the urine which can be measured as increased urinary 17 OH steroid. In the absence of normal anterior pituitary function, the adrenal will not put out increased urinary steroids. As other tests of pituitary function have been developed, it has become clear that this test is not always reliable in demonstrating pituitary insufficiency and indeed may be normal in the presence of other demonstrated pituitary hormonal inadequacies. (The test consists of 750 mg. Metyrapone PO every 4 hrs. for 6 doses. A urine showing double the baseline output of steroid suggests a normal ACTH output.)

Very recently there has been suggestion that aqueous vasopressin 10 units IM may give sharp elevations in plasma cortisol by causing release of ACTH from the anterior pituitary.[9] Normal function is assumed when values showing average elevations of plasma cortisol of 10 mgs.% above baseline occur in 30 minutes of less. It should be pointed out that this test is not yet standardized but may in the future offer a quick and easy screening procedure for pituitary function.

Hopefully, within the next year pituitary growth hormone assays will be available to the Maine physician. Much has been learned regarding growth hormone and its control in the last several years. Sharp rises in plasma growth hormone are demonstrated with sleep, hypoglycemia, activity and arginine stimulation making this a valuable test of pituitary function. Pituitary insufficiency tests of this sort will soon replace Metyrapone and FSH by bioassay.

Armed with the availability of these few tests described in this article the non-endocrinologist can effectively and efficiently deal with and solve 90% of the problems connected with the diagnosis of glandular disorders.

Continued on Page 17

SPECIAL ARTICLE

Who Needs Books?

PHILIP G. GOOD, M.D.*

The intense biomedical research effort of the last twenty years has resulted in an accumulation of new medical knowledge which is overwhelming to contemplate. Much of this research has resulted in readily applicable diagnostic and therapeutic techniques; the communication of these techniques to the practicing physician, however, has been disappointingly slow. Dr. Sidney Farber of the Children's Hospital Medical Center in Boston emphasized this fact when he said at a conference-workshop in Washington D.C. in 1968 "of 300,000 patients who are going to die of cancer this year we could save 100,000 if we could see to it that they all received all that medicine, surgery, and laboratory science has to offer today for their prolongation of life and hopefully for their cure."

There are well conceived and skillfully presented television programs where the physician may view the "latest advances in medical science" at the hospital with his colleagues or better still in the comfort of his home. Films, film strips, and tapes, both audio and video, are extensively offered in attacking this problem of medical communication.

The importance of the message, however, is frequently lost in the glamour of the medium. When the John Hancock Company so successfully advertises its computerized determination of insurance needs and the Maine State Police warn the motorist that he is under surveillance both by radar and computer, the aura of the medium becomes one of almost infallible power. Learning by the prosaic process of merely reading a book seems no match for the sophisticated computer-assisted teaching techniques of today.

In general, information is most useful and more easily retained when the need to know exists. To the front line physician, however, this need is best met by information which is not only immediately applicable but readily available. To date, nothing has replaced the well organized medical library either as a readily accessible repository of knowledge or as a reliable resource for continuing education. Innumerable physician surveys throughout the country have indicated that the physician's primary strength in the search for knowledge is from his reading (notwithstanding the reputedly high place the drug salesman has in a physician's continuing education). The traditionally independent physician relies in most instances on his personal library and journals. The evidence shows that while his own library may be adequate, the library of his workshop, the community hospital, is often quite meager. If the hospital libraries throughout the state were the only source for physician education, the implication would be disturbing. This is obviously not the whole situation but it does suggest that any improvement in library resources would result in greater educational benefits not only to physicians but to their allied health personnel as well.

In July and August of 1969, Maine's Regional Medical Program conducted a library survey of over thirty Maine hospitals, in over one-third library facilities were found to be non-existent. However, in all of these hospitals the interest was high for any activity directed toward improving the medical library. Progress is now being made toward remedying these recognized inadequacies which, by the way, are not unique to Maine but are national in scope.

Probably the most effective catalyst for this steady progression toward library improvement was the Medical Library Assistance Act of 1965. An early effect of this act was the establishment of the Francis A. Countway Library of Medicine in Boston as a New England Regional Medical Library Service (NERMLS), part of a nationwide network of strong established medical libraries able to provide services to the smaller subregional libraries of their area. The physicians, nurses, and allied health workers of Maine are linked to this national system by a teletypewriter exchange (TWX) between the Maine Medical Center, the Countway and the National Library of Medicine. Reference services, training institutes for part-time library supervisors and consultative support for sub-regional libraries have contributed to the success and widespread regional influence of NERMLS. During NERMLS first year of operation, it quickly became apparent that others were also concerned with medical libraries and their place in the communication of medical knowledge. There are at least three agencies which have had and are still having an effect on medical libraries in Maine; namely, the Maine Medical Center, Maine's Regional Medical Program, and the educational division of the Massachusetts Medical Society, known as the Postgraduate Medical Institute (PMI).

The Maine Medical Center with the stimulus provided by a forward looking administration, a vigorous educational department and a strong library committee has taken full advantage of the opportunities presented for improving the medical library resources of the state. In August of 1967, the Center received a federal grant which allowed the library to provide a limited photocopying service and to acquire a wider collection of texts and

*Coordinator, Continuing Professional Education, Maine's Regional Medical Program.

journals. Shortly after obtaining this resource grant a certified medical librarian, Miss Eleanor Cairns, was employed. Her influence has extended well beyond the walls of the hospital. She has conducted training sessions for community hospital librarians, is a member of the subregional medical library task force of NERMLS and is now in the process of organizing an active medical library association for the State of Maine.

In July of 1969, the Maine Medical Center was notified of the approval of its RMP grant request which will allow an expansion of its existing facilities and a strengthening of its role as a subregional library for the entire state. Of particular interest to the physicians of Maine, the grant provides a twenty-four hour toll free, wide-area telephone service line (WATS) which will greatly facilitate photocopying requests and literature searches. An assistant librarian, Mrs. Jane Cooper, has been added to the staff to expedite these services. Elsewhere in this issue the mechanism for utilizing the Maine Regional Medical Library Service, via telephone, is outlined.

The PMI under a Public Health Service Contract has been studying the effect of its consulting services on the development of continuing education in community hospitals. Both this study and the need for a good medical library in the community hospital were important factors in the formation of a profitable alliance between PMI and NERMLS. Together they developed the core medical library concept for the community hospital. Specialists representing fifty areas of medical practice were requested to recommend textbooks and journals in their area of interest. From the results of this survey, a core medical library was selected. This core list consisting of forty-nine books and thirty-eight journals costs somewhat less than $2,000 with an additional $500 per year to keep the library current. Fourteen Maine hospitals are participating in an experimental study to test the effectiveness of this core library. Its reception throughout the region has been enthusiastic, even hospitals who consider themselves too small to afford the total library are beginning to think of at least a modified version.

The need for a true health science library becomes clearly evident as the team rendering health care today becomes larger and more sophisticated. NERMLS and PMI in recognition of this need are developing core libraries for nurses and allied health personnel as well.

In summary then, the medical libraries of Maine through the cooperative efforts of the Regional Medical Program, the Maine Medical Center, NERMLS and PMI are joining a nationwide network of medical communication fulfilling their allotted role as local centers of medical education and information for all members of the health care team.

295 Water Street, Augusta, Maine 04330.

PRACTICAL DIAGNOSTIC ENDOCRINOLOGY FOR THE NON-ENDOCRINOLOGIST – *Continued from Page* 15

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233 Vaughan St., Portland, Maine 04102.

X-Ray Of The Month*

This 17-month-old pale child was hospitalized because of vomiting of one-week duration.

Plumbism

Although the incidence of lead poisoning has greatly decreased in recent years, the clinician is still faced on occasion with a chronically ill child presenting with a history and symptomatology highly suspicious of lead intoxication. Our patient, a 17-month-old pale child, was admitted to the hospital because of persistent vomiting of one-week duration. Of considerable importance in this child's history was his fondness for the paint on the windowsills.

A roentgenographic evaluation of such a patient can be of great value to the clinician in arriving at a rapid diagnosis of lead intoxication. A routine radiologic workup of such a patient should include single projections of the abdomen and extremities.

The plain film of the abdomen will often times demonstrate the opaque lead particles within the gastrointestinal tract. However, the most valuable information is often obtained from radiographs of the extremities and pelvis where dense transverse metaphyseal bands are seen just under the epiphyseal plates. The width of the "lead lines" varies and depends upon the amount of lead ingested and the length of time it has been taken.

In the present case, the lead particles were clearly visualized within the abdomen. The lead lines of the metaphyses are also well seen.

*From the Department of Radiology, Maine Medical Center, Portland, Maine 04102.

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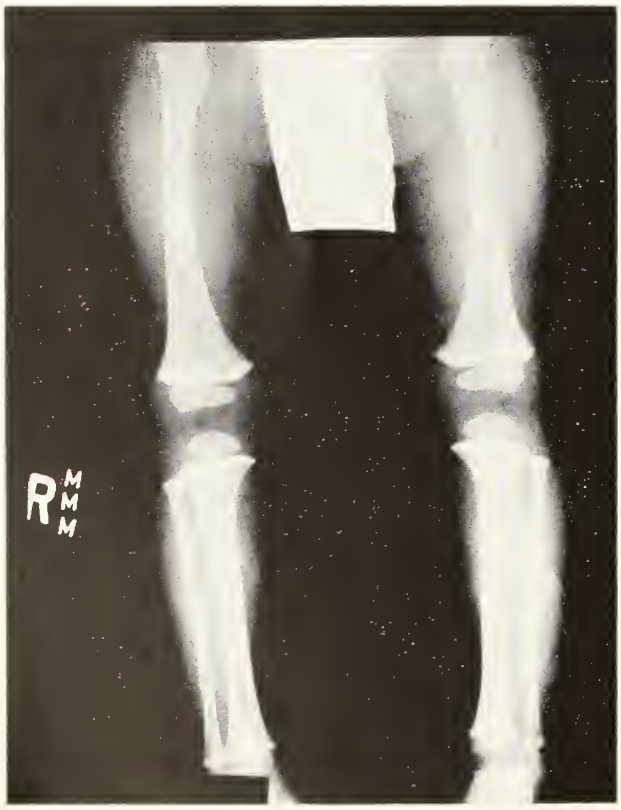

Fig. 1

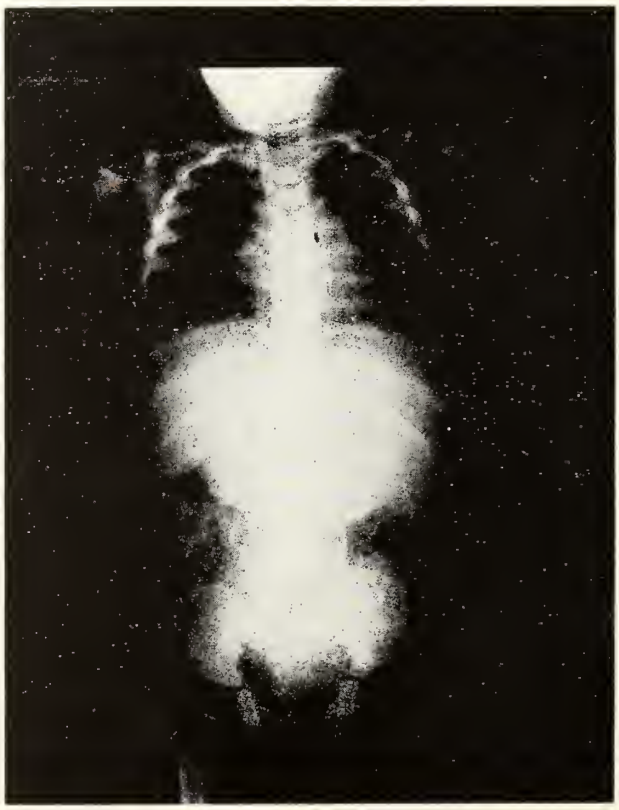

Fig. 2

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Anticoagulants in Acute Myocardial Infarction: The Last (?) Word

Although anticoagulants have been used in the care of patients with acute myocardial infarction for more than 20 years, the efficacy of such therapy has remained in doubt. . . . With the current emphasis on prevention and treatment or arrhythmias, a reconsideration of the role of anticoagulants seems advisable. . . .

Gifford and Feinstein reviewed the methods used in the 27 studies reported in the English-language literature comparing an anticoagulant-treated group with a control group during the acute phase of myocardial infarction. . . . The reviewers concluded that the violation of certain clinical and scientific principles is the source of the current controversy about anticoagulant therapy. They noted that, "for each of the cited methodologic standards, anticoagulant therapy was found superior to no treatment more often in the reports that did not observe the standard than in those that did."

. . . The Working Party on Anticoagulant Therapy in Coronary Thrombosis reported their "Assessment of Short-term Anticoagulant Administration after Cardiac Infarction." Their multicenter prospective trial randomly assigned 1,427 patients to either of 2 groups. . . . The two groups proved to be comparable in age, sex, and number and severity of previous myocardial infarctions. . . . there were no significant differences in the severity of the infarction, the occurrence of reinfarction, the time of ambulation, or the mode or time of occurrence of death. On the other hand, clinical thromboembolic incidents occurred twice as frequently in the token-treated group. . . . Also, hemorrhagic incidents were four times as frequent in the treated group but caused no deaths.

Most important, the total mortality rate was not affected by anticoagulant therapy.

Although the above cited study . . . would fail to meet all eight of the standards set forth by Gifford and Feinstein, it is the largest study yet reported, and it does meet the principal criterion of random assignment of patients in a prospective study with concurrent controls. Several criticisms can be offered . . . It is evident that the degree of anticoagulation used by the Working Party is considerably less intense than that commonly recommended in this country, ... It would appear . . . that none of the criticisms is serious enough to negate the authors' conclusion that for the patients selected the degree of anticoagulation achieved did not affect mortality in acute myocardial infarction.

Thus, the Working Party study would appear to be the most acceptable of all of the studies of anticoagulation in acute myocardial infarction. Although questions can be raised about the efficacy of more intense degrees of anticoagulation . . . , it would appear that the levels of anticoagulation used do not influence mortality and that the routine use of such therapy has again not been supported. The physician therefore may wish to concentrate his efforts on the many other aspects of care for the patient with myocardial infarction.

Submitted by Jacob B. Dana, M.D., Maine Heart Association.
Editorial: Wasserman, A. J.: Annals of Internal Medicine, Vol. 71, pages 855-856, 1969.

AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

Fess Parker 1970 National Cancer Crusade Chairman

NEW YORK, N.Y. — A man of action, TV and film star Fess Parker, will lead over two million volunteers in the American Cancer Society's 1970 Crusade, Chairman of the Board, William B. Lewis, announced at the Society's Annual Dinner in New York City.

The six-foot, six-inch Parker is shouldering the job of topping the record 1969 Crusade total of nearly $60-million. "Crusade is a matter of education as well as fund-raising," Parker said. "ACS volunteers bring vital information about cancer prevention and safeguards to their neighbors."

Serving as Associate National Crusade Chairman will be Mrs. William Talman, widow of actor William Talman who made an unforgettable anti-cigarette ACS TV spot shortly before succumbing to lung cancer. Mrs. Talman will be carrying forward her husband's courageous fight against cancer.

Star and co-producer of the "Daniel Boone" series on NBC-TV, Parker has already made TV spots and a major film for Crusade use. The annual ACS campaign will be launched at a two-day meeting in Chicago in January. He joins the list of distinguished entertainers — Gregory Peck, Lawrence Welk and Virginia Graham — who have taken on the role of national Crusade Chairman.

Parker is a Renaissance man in the complex world of modern show business. A recording artist whose sales hit 500,000 with "Wringle Wrangle," and a million — plus with "Davy Crockett, " he composed "Lonely" and other successful songs. His television credits include involvement with 12 different major shows from "The Dean Martin Show" to the "Ed Sullivan Show." "Old Yeller," "The Great Locomotive Chase" and "Davy Crockett, King of the Wild Frontier," are among his screen efforts.

A man who commutes from his home in Santa Barbara to Hollywood via his own aircraft titled, "Frontier Worlds," Parker enjoys the outdoor life. He rides, hunts, raises horses and sails. At the same time he has a keen interest in education, serving as vice president of the University of Santa Clara Board of Fellows. Parker graduated from the University of Texas and took graduate courses at the University of Southern California until the opportunity to appear with Henry Fonda in the National Company of "Mister Roberts" intervened.

A native of Fort Worth, Texas, whose name, "Fess," means "proud," in Old English, Parker has long been identified with American heroes. In September 1968, he issued a six-cent "Daniel Boone" commemorative stamp for the U. S. Post Office. A month later, he received a Distinguished Alumnus Award from the University of Texas.

In 1960, Parker married the former Marcella Rinehart. They have two children, Fess Elisha Parker III, and Ashley Allen Parker. "I'm working to have a world free of cancer for our children," Parker said.

American Cancer Society News Service Release.

THE COMMITTEE ON CONTINUING EDUCATION of the **AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS** announces its

1970 SCHEDULE of ACADEMY COURSES

Course	Date—City	Producing Committee	Course Chairman
Spinal Disorders in Children	Feb. 28-Mar. 2 Atlanta	Committee on the Handicapped Child	Wood W. Lovell, MD 340 Boulevard, NE., 30312
The Shoulder in Sports	March 9-11 Oklahoma City	Committee on Sports Medicine	Don H. O'Donoghue, MD 1111 N. Lee St., 73103
Orthopaedic Rehabilitation	March 16-18 Chicago	Committee on Orthopaedic Rehabilitation	Clinton L. Compere, MD 737 N. Michigan Ave., 60611
Biomechanics Seminar	May 11-15 Cleveland	Committee on Basic Science	Victor H. Frankel, MD 2065 Adelbert Rd., 44106
The Knee	May 25-28 Boston	Committee on Injuries	William R. MacAusland, Jr., MD 412 Beacon St., 02115
Rheumatoid Arthritic Surgery	June 4-6 San Francisco	Committee on Arthritis	William R. Murray, MD Univ. of Calif. Med. Ctr., 94122
The Knee in Sports	August 3-5 San Francisco	Committee on Sports Medicine	Fred L. Behling, MD 300 Homer Avenue Palo Alto, California 94301
The Hip	Sept. 13-16 Philadelphia	Committee on Adult Orthopaedics	Raymond G. Tronzo, MD 133 S. 36th St., 19104
Sports Medicine	Sept. 28-30 Buffalo	Committee on Sports Medicine	Joseph D. Godfrey, MD 77 Bryant St., 14209
The Critically Ill Orthopaedic Patient	Oct. 21-23 Boston	Committee on Injuries	Henry H. Banks, MD 721 Hunting Ave., 02115
Biomechanics Seminar	Nov. 9-13 Cleveland	Committee on Basic Science	Victor H. Frankel, MD 2065 Adelbert Rd., 44106
The Upper Extremity	Nov. 18-20 Los Angeles	Committee on Injuries	J. Paul Harvey, Jr., MD 1200 N. State St., 90033
Myelomeningocele	Nov. 22-24 Hartford	Committee on the Handicapped Child	Burr H. Curtis, MD 181 E. Cedar Street Newington, Connecticut 06111
The Lower Extremity	Dec. 7-9 Miami	Committee on Injuries	Augusto Sarmiento, MD Jackson Memorial Hospital, 33136

Courses are designed for orthopaedic surgeons but are open to other interested physicians and allied health personnel. For further information, contact the Coordinator of Continuing Education, American Academy of Orthopaedic Surgeons, 430 North Michigan Avenue, Chicago, Illinois 60611 • (312) 822-0970.

REGISTRATION LIMITED

REGISTRATION LIMITS will be set by the Course Chairman to avoid overcrowding of Course facilities. The Preliminary Program will be mailed three to four months prior to a Course and will contain the necessary advance registration information.

Report of Delegate to 1969 AMA House of Delegates Clinical Meeting

George W. Wood, III, M.D.

The Clinical Meeting of the AMA was held in Denver, Colorado, from November 30 to December 3, 1969. There were twenty-two reports from the Board of Trustees; three special reports; one from the Council on Constitution and Bylaws; five from the Council on Medical Education; two from the Council on Medical Service; and sixty-six Resolutions.

The Delegate has already discussed with the Council various aspects of this most important session which marked another step in the re-orientation of the AMA.

The sixty-page report of the Committee on Planning Development and its associated minority report were the central features of the meeting. This is to be furnished all members of the Council of the Maine Medical Association, and, if acceptable to this Council, should be forwarded to all members of the House of Delegates of our Association. From this, the Maine physician may decide his particular attitude on the various factors discussed. If the House desires resolutions to be presented at the annual meeting in Chicago, these may be formulated.

The Maine delegate was pleased to see that the Institute for Bio-medical Research was phased out as an AMA project. Instead of this academic emphasis, it would seem AMA is now concerning itself more with medical care of *all* of society. This interest and enthusiasm was manifested in the reception afforded the report on health care of the poor.

I am sure that Dr. Charles Branch's presence added to the value of this clinical meeting. Unfortunately, the alternate delegate, Dr. Richard Laney, was unable to attend but it is hoped that he will return to the battle in the Chicago meeting.

Thank you for this opportunity to serve, particularly in this era of exciting, and, hopefully, constructive change.

County Society Notes

WASHINGTON

The regular meeting of the Washington County Medical Society was held on September 29, 1969 at the Dennys River Inn, Dennysville, Maine with thirteen members and guests present.

Irwin M. Pasternak, M.D., a Psychiatrist from Bangor spoke on the Cycle Psychopharmacology of Tranquilizers. Dr. Pasternak outlined the office use of the major tranquilizers, including the Dimethylaminopropyl, such as Thorazine®, Sparine® and Vesprin®; the Piperidyl compounds, such as Mellaril®; and the Piperazine compounds, Prolixin®, Trilafon® and Compazine®, Stelazine® and Dartal®; and Taractan® which is a major tranquilizer, but not a phenothiazine. He discussed the advantages and disadvantages of the various types of drugs with some of the side effects, which might be expected, such as the extra pyramidal action. This syndrome may be manifested by Parkinsonism or by dyskinetic reactions or akathisia which is manifested by inability to sleep and continual restlessness. Much of this can be controlled by use of antiparkinson's drugs, such as Artane® or Cogentin®. Some physicians give these drugs at the same time they give the tranquilizers.

Dr. Pasternak explained the use of some of the minor tranquilizers, such as Meprobamate®, Librium®, Vistaril®, Atarax®, Valium® and Serax®. He also covered the use of some of the anti-depressants, such as Tofranil® and Elavil®, and said many monoamine oxidase inhibitors were no longer used. He also spoke of the use of the amphetamine compounds in hyperkinetic children.

This excellent talk was followed by a business session.

A letter was read from the Senior Citizen's of Washington County, asking that the doctors prescribe generic medication. They asked that one of their members be allowed to speak to the Society. It was voted to invite their representative to speak to us at the next meeting.

It was brought to the attention of the members that the 1970 annual session of the Maine Medical Association will be held at The Colony, Kennebunkport, Maine, June 7, 8 and 9. It was brought to the attention of the members that those who had not contributed to the Maine Medical Education Foundation should do so immediately.

A letter was read from Walter A. Mendyka, M.D. notifying the Society of his resignation as President of the Society because of his transfer to a physicians' group in West Springfield, Massachusetts as of September 1st.

The Society welcomed Nelson Stott, M.D. of Eastport, Maine, formerly of Halifax, Nova Scotia, as a new member.

The following officers were elected:

President, George B. Shaw, M.D., Machias
Vice President, Joseph B. Kiel, M.D., Columbia Falls

The Washington County Medical Society meeting was held on October 27, 1969 at the Dennys River Inn, in Dennysville, Maine, with eight members and guests present.

A business meeting of the Society was presided over by the Vice President, Joseph B. Kiel, M.D.

At the next meeting, it was voted to elect a delegate and alternate plus two members to the Board of Censors. At the next meeting, also, John C. Van Pelt, M.D. a Pediatrician from Ellsworth, will speak to the Society.

Following the business meeting, five representatives of the Senior Citizens of Washington County spoke to the Society, relative to prescribing generic drugs. The representatives of the Senior Citizens stated their feeling that generic drugs should be used whenever possible, because of the financial saving to themselves. The physicians stated that they would use generic drugs whenever possible, but due to certain patent rights, it was not always possible to use generic drugs. The physicians also felt that they were not as well acquainted with some of the generic drugs, as they were with the name brands

and felt that it would not be to the best interest of the patient to prescribe the generic drugs many times. The physicians asked the members of the Senior Citizens to state to their various members that they would be quite willing to prescribe generic drugs, but it would be up to the Senior Citizens to ask their physicians if he could possibly prescribe a generic drug.

A meeting of the Washington County Medical Society was held on November 24, 1969 at the Dennys River Inn in Dennysville, Maine.

Charles F. Branch, M.D., President of the Maine Medical Association, spoke to the Society relative to plans of the Maine Medical Association as a group. Dr. Branch said that lately there had been much interest in the future of medical practice and more particularly the medical practice as it would affect doctors in the State of Maine. A group had been formed and had reported their ideas as to how we could best work together, as a unit, to control our own practice in medicine and not have it completely controlled by third party groups. Dr. Branch felt that if all physicians would cooperate this could probably be accomplished.

Nelson W. Stott, M.D. of Eastport, Maine said that in Nova Scotia that they had had good experience with hiring Public Relations personnel, so that the general public would have a better idea of what the physicians were actually doing.

John C. Van Pelt, M.D., a Pediatric Neurologist of Ellsworth, Maine spoke on "Seizure Disorders." Dr. Van Pelt covered grand mal, petit mal and psychomotor type of seizures. He also spoke on the various type of so-called "minor motors seizures" such as Myoclonic seizures, head nodding and Akinetic seizures as well as Febrile seizures and such things as "breath holding." He covered the treatment of the various types of seizures. He felt that it is best always to start with one drug at a time, and usually Phenobarbital was the first drug to use, given until there were signs of "toxicity," if no affect, then the dose reduced and another drug, such as Dilantin® added. He said with Phenobarbital it was possible to give just one dose at bedtime, and that Dilantin could be given once or twice daily. He felt that any drug should be used two weeks before changing or starting another type of drug. Dr. Van Pelt felt that the use of various types of liquid mixtures particularly with Dilantin, were probably hazardous because of the fact that the dose could not be titrated exactly. Dr. Van Pelt then talked on "Electroencephalography." He demonstrated where the various electrodes should be placed. He then demonstrated and showed the results of eight point lead; a normal, a patient that was drowsy, a patient that was asleep, a patient with a petit mal, grand mal, psychomotor seizure and one from a patient that had had a massive cerebral vascular accident. He said that it was not an exact science, and it was only an aid, and not always diagnostic.

Donald M. Robertson, M.D. of Milbridge, Maine was elected to serve as a delegate to the Maine Medical Association House of Delegates and Robert G. MacBride, M.D. of Lubec, Maine as an alternate delegate.

KARL V. LARSON, M.D., *Secretary*

KENNEBEC

The Kennebec County Medical Association met at the Holiday Inn in Augusta, Maine on October 16, 1969, with forty-eight members and guests present. Following the social hour and dinner, the business meeting was called to order by the President, Joseph R. Crawford, M.D.

Dr. Crawford introduced Norman E. Cobb, M.D. of Belfast, Councilor for the Fourth District and John R. Webber, M.D. of Belfast, a member of the Waldo County Medical Association.

David L. Ebersbach, M.D. of the Brunswick Naval Air Station was elected to membership.

The scientific program of the evening was given by Hugh Johnston, M.D. of the Research Laboratory, Maine Medical Center. Dr. Johnston's topic was "The Clinical Use of Steroids." Dr. Johnston presented a most informative and excellently illustrated discussion of the use of these agents presented from the point of view of an endocrinologist. A discussion period followed.

FRANCIS A. SPELLMAN, M.D., *Secretary*

PENOBSCOT

The Penobscot County Medical Society meeting was held at the Millinocket Community Hospital in Millinocket, Maine on October 21, 1969 with the President, Lloyd Brown, M.D., presiding.

Earle M. Davis, M.D., Urologist, of Waterville, Maine presented several interesting urological cases, and there was general participation in a discussion of urinary tract infections. A business meeting followed the discussion.

A communication regarding Health Insurance fees was read, and this referred to the AMA newsletter, June 30, 1969.

An AMA policy statement on Osteopathy was brought to the attention of the membership. This will be posted and distributed. Russell M. Lane, M.D. remarked that in 1966 it was determined not unethical to extend ancillary and consultative services to Osteopaths, and in 1969 a Resolution was passed instructing the Council to prepare the necessary amendments to the Constitution and Bylaws for acceptance of qualified Doctors of Osteopathy, for presentation in the manner prescribed for presentation to and action by this House at its regular annual session in 1970.

Bourcard Nesin, M.D. spoke in behalf of local physicians who see the need for a hospital facility in the Lincoln area. He made two points: 1) Strong support is needed from the M.M.A. and regional planning committees; 2) Osteopathic physicians must be included in a cooperative arrangement.

John J. Pearson, M.D., in a communication, questioned apparent weaknesses in the Implied Consent Law, and also suggested that a physicians' fee be established. This was discussed and it was moved that a committee (Drs. Pearson, Chairman, Thornton W. Merriam, Jr. and Hans A. Holzwarth) study the law and bring in a resolution for the executive council and possibly for the House of Delegates to consider.

Committees were appointed to bring in resolutions on John E. Burke, M.D. (Drs. Edward L. Curran, Robert J. Barrett, Jr. and Richard T. Munce) and Magnus F. Ridlon, M.D. (Drs. John E. Whitworth, Asa C. Adams and Allison K. Hill).

An announcement of the following delegates and alternates to the 1970 Maine Medical Association House of Delegates was made:

Delegates: Drs. John J. Pearson, Old Town; Herbert C. Gilman, Millinocket; Leonard G. Miragliuolo, Thornton W. Merriam, Jr. and Stanley J. Evans, all of Bangor. Alternates: Drs. Wilfred I. Butterfield, Lincoln; Russell M. Lane, Orono; George O. Chase, John F. McGinn and J. Robert Feeley, all of Bangor.

WILLIAM M. SHUBERT, M.D., *Secretary*

ANDROSCOGGIN

A joint meeting of the Androscoggin County Medical Association and the Androscoggin County Bar Association was held on October 22, 1969 at Steckino's Restaurant in Lewiston, Maine. The President, John W. Carrier, M.D., presided.

The guest speaker was Dennis M. Mahoney, M.D. of Denver, Colorado. Dr. Mahoney spoke of the need to obtain patient consent before taking certain actions on the patient. Dr.

Mahoney, who is both a practicing physician and an attorney, cited histories of cases in which the doctor had not obtained, in writing, permission from the patient to perform certain operations or other acts. His talk was on "Implied Consent," but was not in any way connected with Maine's new Implied Consent Law. He warned doctors to make sure before they perform certain acts that they have the patient's permission in writing from the patient himself. He told the physicians not to rely on a nurse or an assistant to obtain permission, but for the physician himself to do it.

The meeting of the Androscoggin County Medical Association was held at the Central Maine General Hospital in Lewiston, Maine on November 20, 1969, with twenty-two members present. The meeting was called to order by the President, John W. Carrier, M.D.

Drs. Miguelito A. Cabelin, Frederick C. Holler, Yasuo Kanda, Joseph P. Fanning, Raymond E. O'Keefe and Richard M. Swengel were elected to membership at a previous meeting held jointly with Lawyers at Steckino's.

Waldo A. Clapp, M.D. read a resolution on the death of Donald H. Horsman, M.D. It was voted to inscribe a copy on our records and send a copy to the family and to the Maine Medical Association.

Dr. Carrier introduced the guest speaker, Mr. Cathgart, Representative of Professional Relations, Blue Shield (liaison between Blue Shield and Physicians). Mr. Cathgart outlined the present status of contracts that are in effect. The different percentage of payment in the Champus program between active duty and retired personnel was pointed out; patients may be billed for balance. Other services that Champus pays for were enumerated. (This in contrast to Blue Cross-Blue Shield and also Federal.) Usual customary and reasonable fees were defined. It was explained how the company arrived at these figures (amounts). The Federal High and Low option Blue Shield program was explained. Benefits not usually covered in standard Blue Shield coverage were discussed. Major medical and extended care benefit contracts under Blue Alliance were mentioned as was a new R Contract started October 1, 1969; only 135 G.M. employees under this so far. He made a plea to physicians to contact Blue Shield if there are any gripes or misunderstandings. A question and answer period followed.

A nominating committee was appointed which consisted of Drs. Stanley D. Rosenblatt, Chairman, Frederick B. Lidstone and Jou S. Tchao.

DONALD L. ANDERSON, M.D., *Secretary*

LINCOLN-SAGADAHOC

A meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on November 18, 1969. The meeting was called to order by the President, Paul A. Fichtner, M.D.

Following the reading of the minutes of the last regular meeting, a birthday cake was then brought in to Francis A. Winchenbach, M.D.

Dr. Fichtner introduced Charles F. Branch, M.D., President of the Maine Medical Association, who greeted the members cordially and posed questions about the future direction of development of the Maine Medical Association.

Dr. Fichtner read the Maine Medical Association list of members of this Society and some changes were made in the designation of types of practice.

Francis A. Winchenbach, M.D. was unanimously recommended for another three-year term on the Maine Medical Association's Health Insurance Committee.

Frank O. Avantaggio, Jr., M.D. moved that this Society donate a sum of money, the amount to be determined at the December meeting, to the Maine Caddie's Association Scholarship Fund, in recognition of the many years of service of Dr. Winchenbach. The motion was seconded and passed unanimously.

Henry A. Hudson, M.D. introduced the guest speaker of the evening, Richard T. Chamberlin, M.D. of Waterville. Dr. Chamberlin showed slides and spoke on Regional Health Facilities Planning, as it applies to the Upper Kennebec Valley.

GEORGE W. BOSTWICK, M.D., *Secretary*

CUMBERLAND

A meeting of the Cumberland County Medical Society was held on November 20, 1969 at Valle's Steak House in Portland, Maine, with eighty-three members and guests in attendance. Guests included Robert F. Ficker, M.D., Councilor for the First District of the Maine Medical Association and Dr. Tom Glascow, Physician-in-Chief at the US Induction Center, Portland, Maine. The meeting was also attended by one member of the House Staff of the Mercy Hospital.

Following dinner, the meeting was called to order by the President, George F. Sager, M.D. Dr. Ficker was introduced and acknowledged his introduction with a brief statement to the Society.

Drs. Thaddeus Kostrubala, Melissa A. Weekley and Philip J. Villandry were elected to membership. The Society voted to nominate Drs. Winifred W. Curtis and Isaac M. Webber to honorary membership.

Thomas A. Martin, M.D. read a resolution on the death of Edward G. Asherman, M.D. A copy of this resolution will be spread upon the record of the Cumberland County Medical Society.

Ferris S. Ray, M.D. reported on the Maine Medical Education Foundation. He reported that ninety-five students are going to medical school from the State of Maine and that forty-four loans were made by the Foundation this year. However, he pointed out that the number of Doctors giving to the Foundation has decreased and this at a time when the Foundation needs more money.

Richard C. Dillihunt, M.D. announced through Dr. Sager that a search is underway for a Director of the Emergency Division at the Maine Medical Center. Anyone knowing of, or wishing to talk about this position should contact Dr. Dillihunt.

Dr. Sager announced the nominating committee had been formed and consisted of Drs. Eugene P. McManamy, Chairman, Charles W. Capron and William F. Taylor.

Lloyd G. Davies, M.D., Vice President of the American Academy of General Practice, was acknowledged.

It was announced to the membership that the annual meeting of the Maine Medical Association will be held at The Colony in Kennebunkport in June, 1970.

It was moved, seconded and voted that the House Officer names be removed from the mailing list of the Cumberland County Medical Society.

Dr. Sager then introduced Daniel F. Hanley, M.D., Executive Director of the Maine Medical Association, who spoke to the Society on "What's Important?" Dr. Hanley listed the following bibliography as one which would be of interest to the Society members to read:

1. THE WHITE HOUSE REPORT ON HEALTH NEEDS – NY Times, 118:40c, July 11, 1969.
2. SCIENCE AND HEALTH CARE – NEJM, 10/16/69, Vol. 26.
3. MEDICAL NEWS REPORT – Vol. I, No. 7, 8 & 9.
4. FUTURE OF MEDICINE – John Millis, JAMA, 10/20/69.
5. "WHAT'S IMPORTANT?" – George Wood, III, M.D. JMMA, 12/69.

Dr. Hanley touched on some of the points in his talk. The question of the patient's right to care is no longer a problem. The problems now are the right to have care for whom?, the quality of care administered, the availability of care, and the

increasing right for care. The demand for care has created an increasing rising spiral of medical care costs so that this year the physicians' fees have increased 7%, or more than twice the cost of living. The biggest purchaser of medical care is the Federal Government and the Federal Health Budget becomes bigger each year. The United States is changing from a production and manufacturing economy to a service economy. Dr. Hanley expressed the feeling that the State medical society should have utilization and review teams. For, the importance of regulating and maintaining standards within our own organizations will help to keep them strong and will eliminate the need for someone else to do it for us. In the end, Dr. Hanley stated that what's important is attention to detail in the management of the patients.

DOUGLAS R. HILL, M.D., *Secretary*

HANCOCK

A meeting of the Hancock County Medical Society was held at the Brookside Restaurant in Ellsworth, Maine on October 8, 1969, with five members and six guests present.

Joseph B. Kiel, M.D. of Columbia Falls, Maine gave a presentation entitled "Psychiatry in Outreach Areas." Dr. Kiel has returned from six years of training in the vicinity of Dallas, Texas and has practiced psychiatry since June in this area. His talk related to services he hoped to give the physicians and the people in this area in his concern for better inter-personal relations at all levels of our Downeast society. He coupled his talk with a brief summary of the development of the personality which requires social interaction.

Mr. Albert Dietrich of Orrington, Maine gave an interesting history of the formation of the Guidance Center in Bangor following Dr. Kiel's talk. The Center was formed in 1968 by the joining of the Eastern Maine Guidance Center with the Family and Child Service in 1968. The Center received a grant of $232,000.00 in July 1969 to serve the mental health needs of a population of 230,000 in Area 2 that includes most of seven counties on a formula that decreases support over a 51-month period. The six elements of service are as follows:

1. Outpatient Service – (a) Counseling: marriage, school problems, personal adjustment; (b) Psychometric testing and evaluation.
2. Inpatient Service – Fourteen Eastern Maine Medical Center beds which will soon be expanded to 22 with an anticipated total of 40. Psychiatrist in charge of this service is Irwin M. Pasternak, M.D., two psychiatric nurses and a psychologist.
3. Day Care, partial hospitalization – A building is being readied for this service which will hopefully be started soon.
4. Education and Consultation – Stress on preventive mental health and involving parents and teachers using movies, speeches, symposia, etc. Two school mental health consultants with Master's degrees in education; two pastoral counselors.
5. Twenty-four hour Emergency Service – Using wide area dialing phone service. Mr. Dietrich mentioned that at least one portion of Area 2 has a suicide rate of over twice the national incidents.
6. Research and Evaluation with the Agency as a guide to progress.

The services of the Center are on a fee basis graduated to the ability to pay. Many of the above activities await the acquiring of proper personnel which is proceeding rapidly at this time. An effort is being made to hire six more psychiatrists.

The Hancock County Medical Society met at the Brookside Restaurant in Ellsworth, Maine on November 12, 1969, with thirteen members and one guest present.

John C. Van Pelt, M.D., Diabetes Detection Week Chairman, announced the activities planned for Hancock County.

Randall H. Silver, M.D. mentioned the controversial Blue Shield-Blue Cross fee schedule. The suggestion was made by members that a guest speaker from the professional staff of the Associated Hospital Service of Maine be invited for discussion of fees with the Hancock County Medical Society.

The President, Winston G. Stewart, M.D., began the discussion of "Medical Politics" by introducing several topics of local, state and federal aspects of health care. This was followed by a lively and wide-ranging commentary in which all members participated. The sense of the meeting was optimistic and enthusiastic for new experimentation while perserving the best in medical care. Mr. Alan Shanske, fourth-year medical student visiting Dr. Lambdin's pediatric service in Ellsworth from the Albert Einstein Medical School, guest at the meeting, commented upon the social aspects of medical care as he had seen them in Hancock County and in Brooklyn, New York.

BRADLEY E. BROWNLOW, M.D., *Secretary*

SOMERSET

The following officers were elected for 1970:

President, Carlton E. Swett, M.D., Skowhegan
Vice President, Vincente L. Sy, M.D., Bingham
Secretary-Treasurer, John P. Dow, M.D., Pittsfield
Delegates to the M.M.A. House of Delegates: Drs. H. Carl Amrein, Madison and Harland G. Turner, Norridgewock. Alternates: Drs. Edgar J. Smith, Fairfield and W. Edward Jordan, Jr., Skowhegan
Credentials Committee: Drs. Andrew M. Szendey, Madison, Howard L. Reed, Skowhegan and George E. Sullivan, Fairfield
Program and Scientific Committee: Drs. W. Edward Jordan, Jr., Skowhegan and Marion L. Strickland, Canaan
Diabetes Detection Drive: Harland G. Turner, M.D.
Ethics and Grievance Committee: Drs. Louis S. Hornstein, Skowhegan, George E. Sullivan and John P. Dow

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News, Notes and Announcements

Symposium
Augusta General Hospital, Augusta, Maine
February 6 and 7, 1970

Symposium
THE PROBLEM-ORIENTED RECORD AS A BASIC TOOL MEDICAL RECORDS, MEDICAL EDUCATION AND PATIENT CARE
Francis J. O'Connor, M.D., Symposium Director

Friday evening, February 6
St. Paul's Oblate Center, 136 State St., Augusta, Maine
5:30 to 6:00 P.M. – Preliminary Registration
6:00 to 7:00 P.M. – Reception
7:00 P.M. – Dinner
8:30 P.M. – Meeting of Symposium Faculty

Saturday, February 7
Augusta General Hospital
8:30 to 9:00 A.M. – Registration, Main Conference Room
9:00 to 5:00 P.M. – All day session

Saturday evening, February 7
St. Paul's Oblate Center
6:00 P.M. – Dinner
Guest speakers: B. Harvey Minchew, M.D., Director, Columbia Health Foundation, Columbia, Maryland and Lawrence L. Weed, M.D., Professor of Medicine, University of Vermont Medical School

Cost of Symposium including meals $15.00.
Cost of the Symposium including meals and room at the Center two evenings $25.00.

Two-Week Review Course in Orthopaedics
July 12-25, 1970
Colby College, Waterville, Maine

The Fourth Two-Week Review Course will be held July 12-25, 1970. Doctors William T. Green and Carroll B. Larson will be co-directors. Inquiries concerning this Course may be addressed to Allan J. Stinchfield, M.D., executive director of the Course or John B. Simpson, director of special and summer courses, Colby College, Waterville, Maine 04901.

Self-Employed Physicians Now Insured For Disability Under Social Security

Many self-employed physicians reached an important social security landmark this October. With their earnings covered since 1965, they have now contributed to social security long enough to be insured for disability.

Social security disability benefits can be paid to an insured person under 65 who has a physical or mental impairment so severe as to keep him from doing any substantial work for a year or longer. Payments begin after a waiting period of 6 full calendar months.

Benefits can be as much as $218 a month for a disabled person alone and up to $434.40 a month for a family. Self-employed physicians disabled in the immediate future, however, would probably not yet be eligible for these maximums since their earnings have been covered by social security for a relatively short time. Benefits are figured from a person's average covered earnings over a period of years.

"This disability protection can be a valuable supplement to the physician's private insurance," said Bernard Popick, director of social security's disability program. "It is part of the total social security package of protection – disability, retirement, survivors and health insurance – toward which the physician has been contributing."

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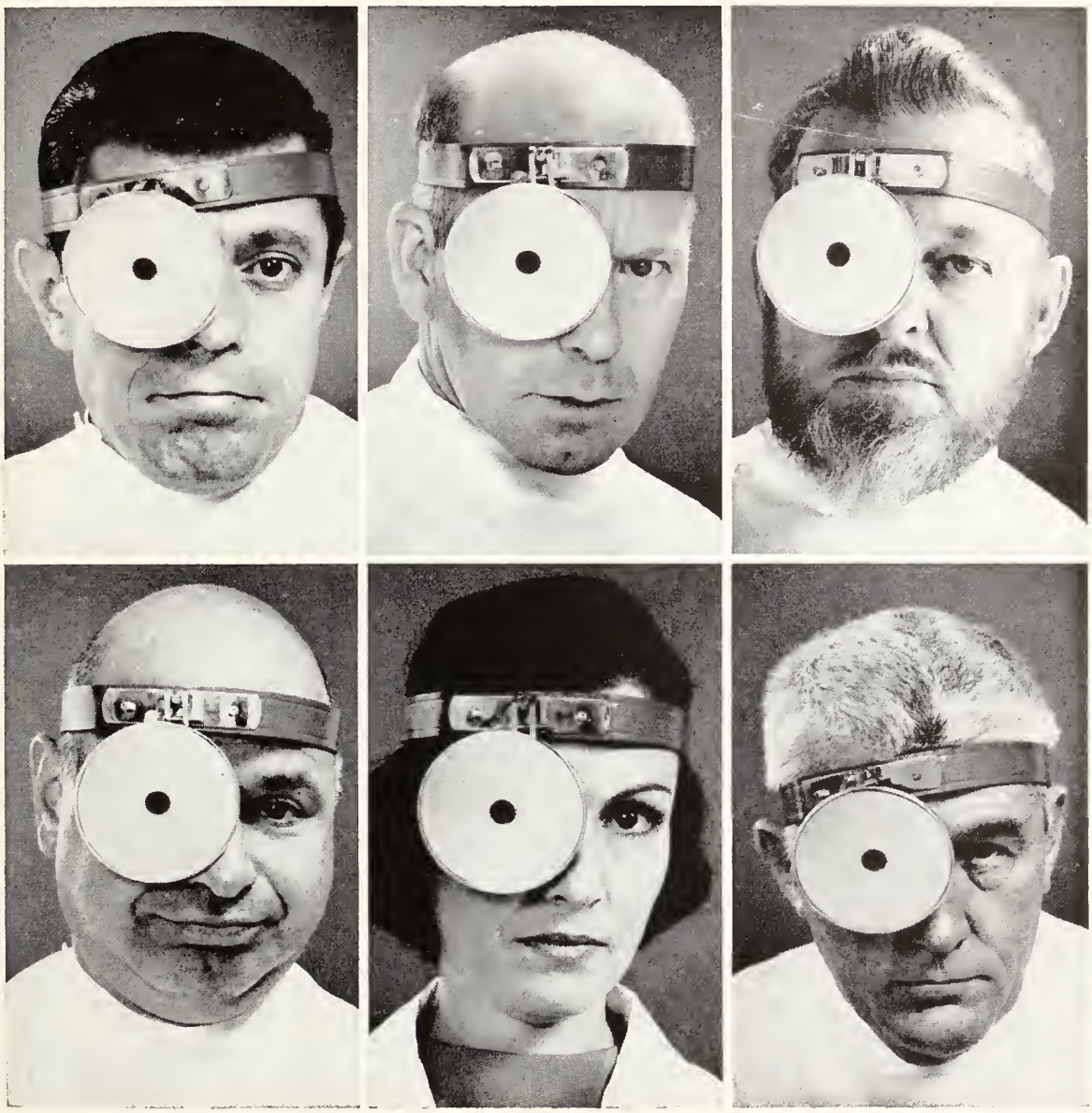

"All Otolaryngologists are Alike"

Just look at them and you can see how much they have in common. Besides, they all go through pretty much the same training, and pass the same kinds of tests, and measure up to the same sort of standards. Therefore, all otolaryngologists are alike. Right?

Wrong! But that's no more preposterous than what some people say about aspirin. Namely: since all aspirin is at least supposed to come up to certain required standards, then all aspirin tablets must be alike.

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These Bayer standards result in significant product benefits, including gentleness to the stomach and product stability, that enable Bayer Aspirin tablets to *stay* strong and gentle until they are taken.

So next time you hear someone say that *all* aspirin tablets are alike, you can say, with confidence, that "it just isn't so."

You might also say that all otolaryngologists aren't alike, either.

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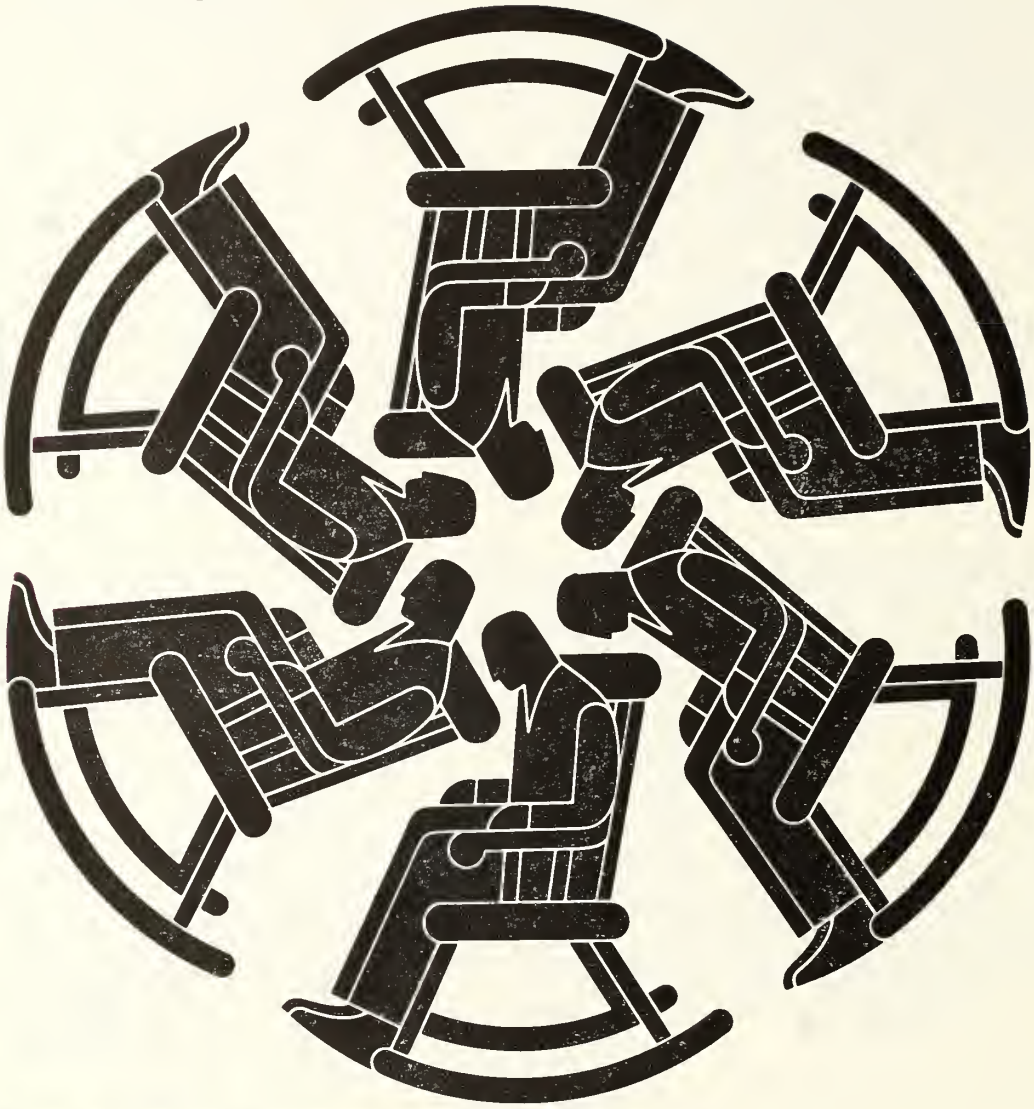

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Usual dosage is one tablet b.i.d.

Indications: Nutritional supplementation in conditions in which water-soluble vitamins are required prophylactically or therapeutically.

Warning: Not intended for treatment of pernicious anemia or other primary or secondary anemias. Neurologic involvement may develop or progress, despite temporary remission of anemia, in patients with pernicious anemia who receive more than 0.1 mg of folic acid per day and who are inadequately treated with vitamin B_{12}.

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Contraindications: Severe central nervous system depression, comatose states from any cause, hypertensive or hypotensive heart disease of extreme degree.

Warnings: Administer cautiously to patients who have previously exhibited a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides. During pregnancy, administer only when necessary.

Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy may be avoided by remaining within the recommended limits of dosage. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving). Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension. Daily doses in excess of 300 mg. should be used only in severe neuropsychiatric conditions.

Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—Changes in the terminal portion of the electrocardiogram have been observed in some patients receiving the phenothiazine tranquilizers, including Mellaril (thioridazine). While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing electrocardiographic changes. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. *Other*—A single case described as parotid swelling.

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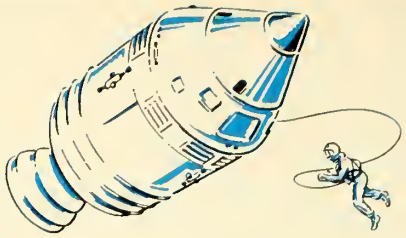

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Important Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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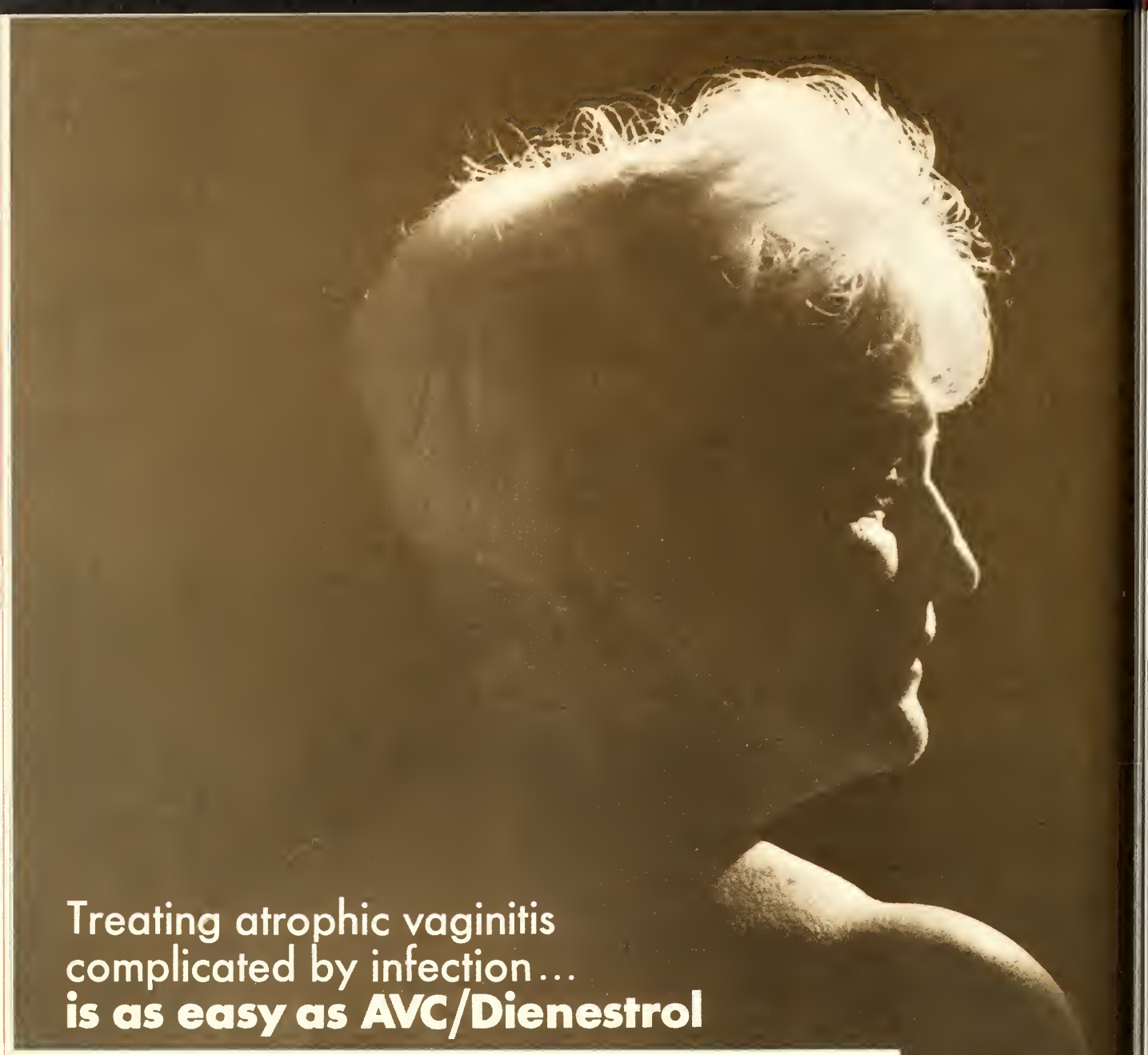

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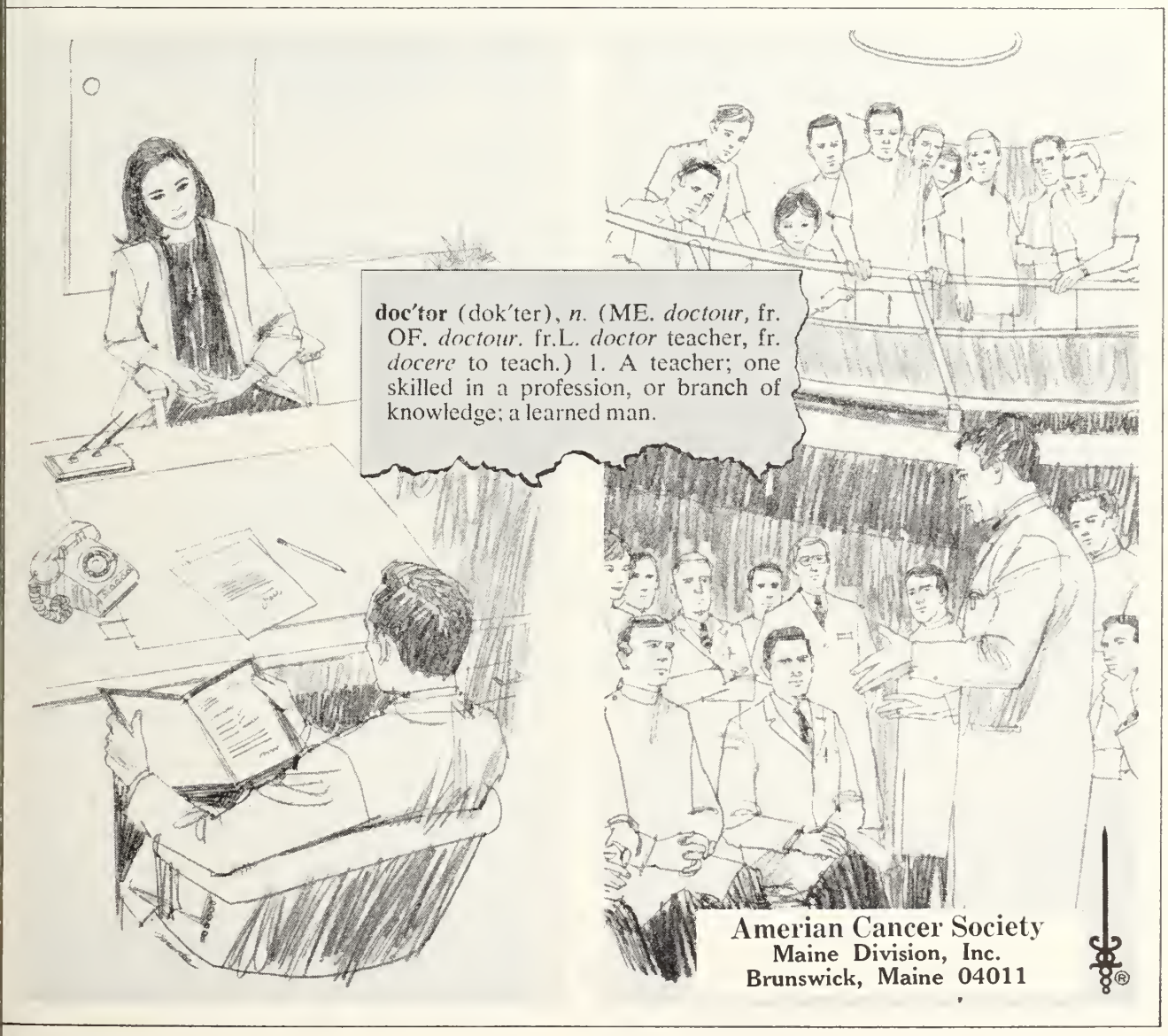

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.*: Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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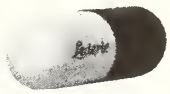

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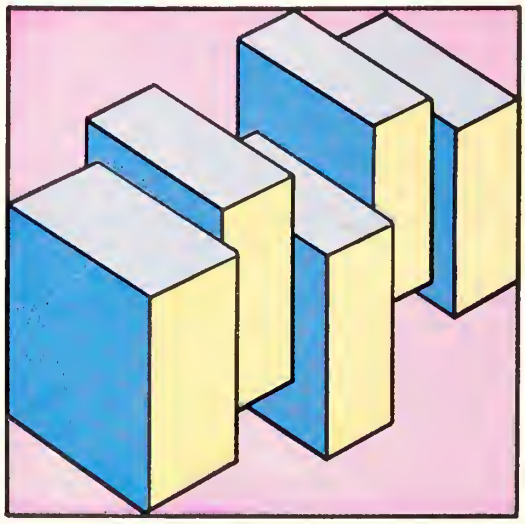

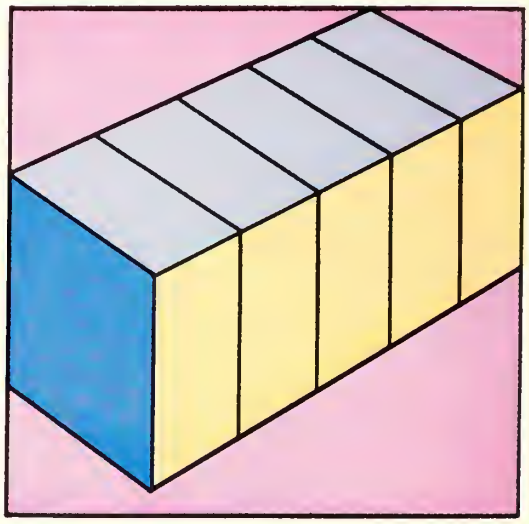

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PRECAUTIONS: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.
ADVERSE REACTIONS: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido--all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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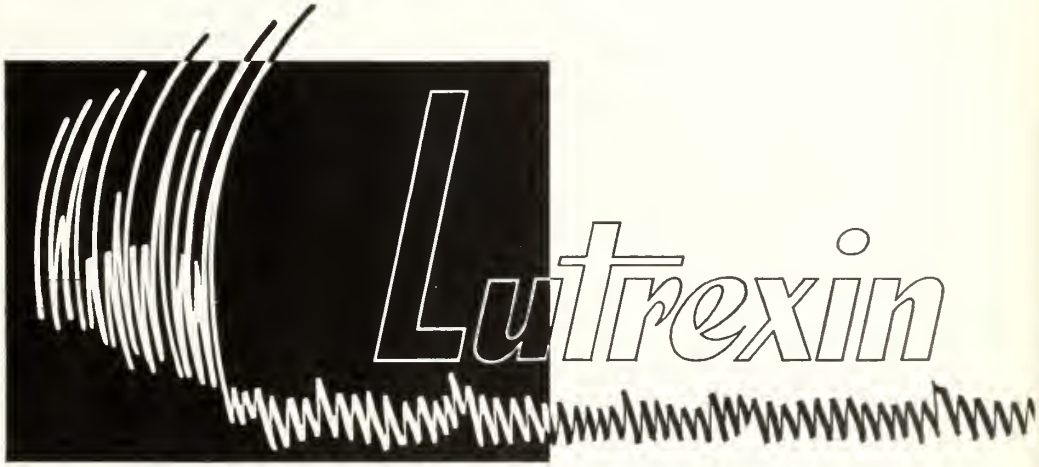

(In vivo measurement of Lutrexin on contracting uterine muscle of the guinea pig.)

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* ESTHER M. KENNARD, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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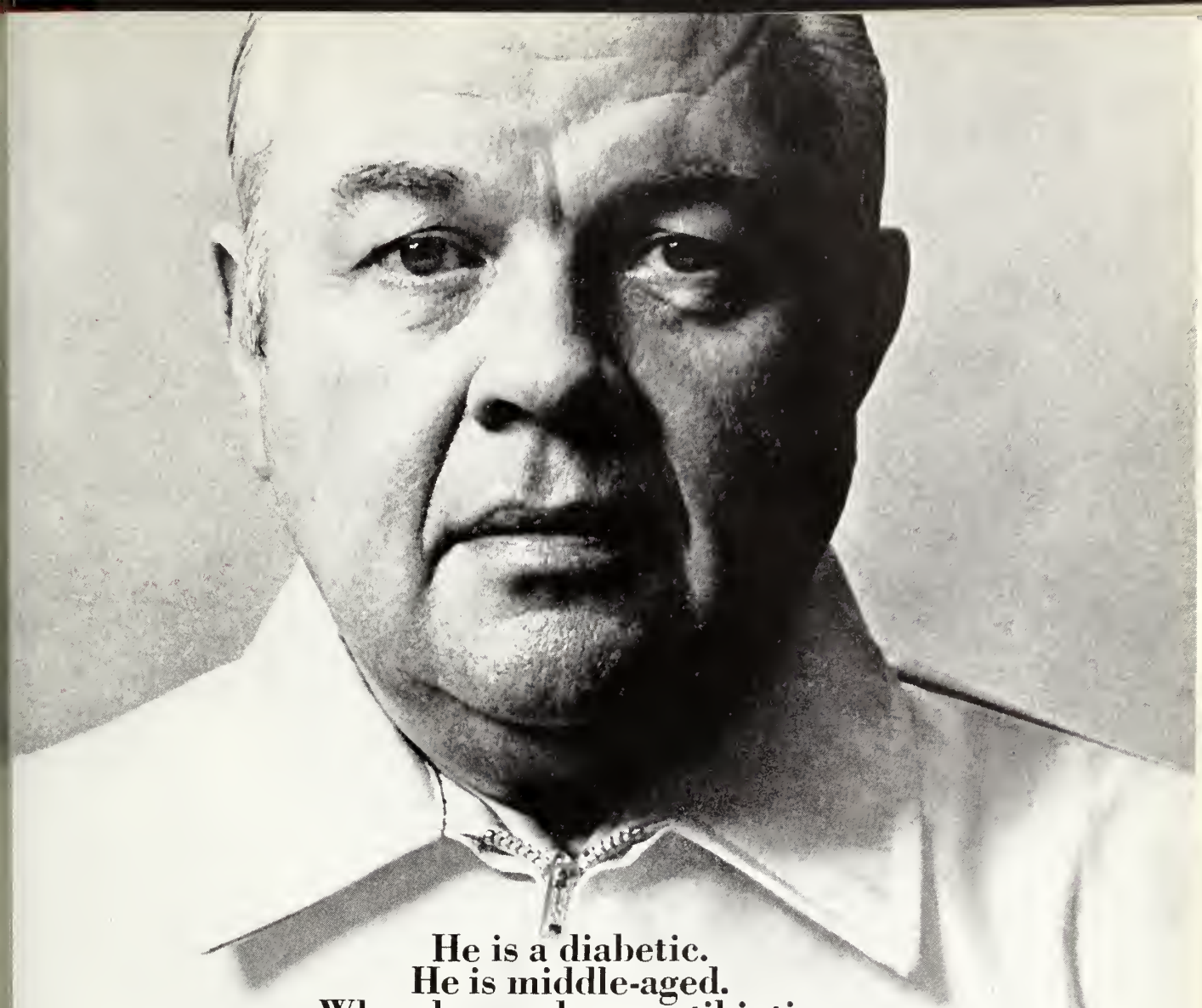

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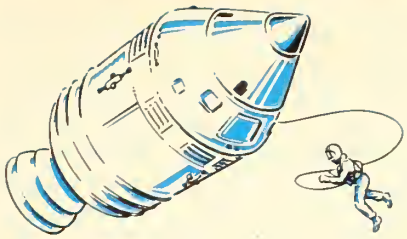

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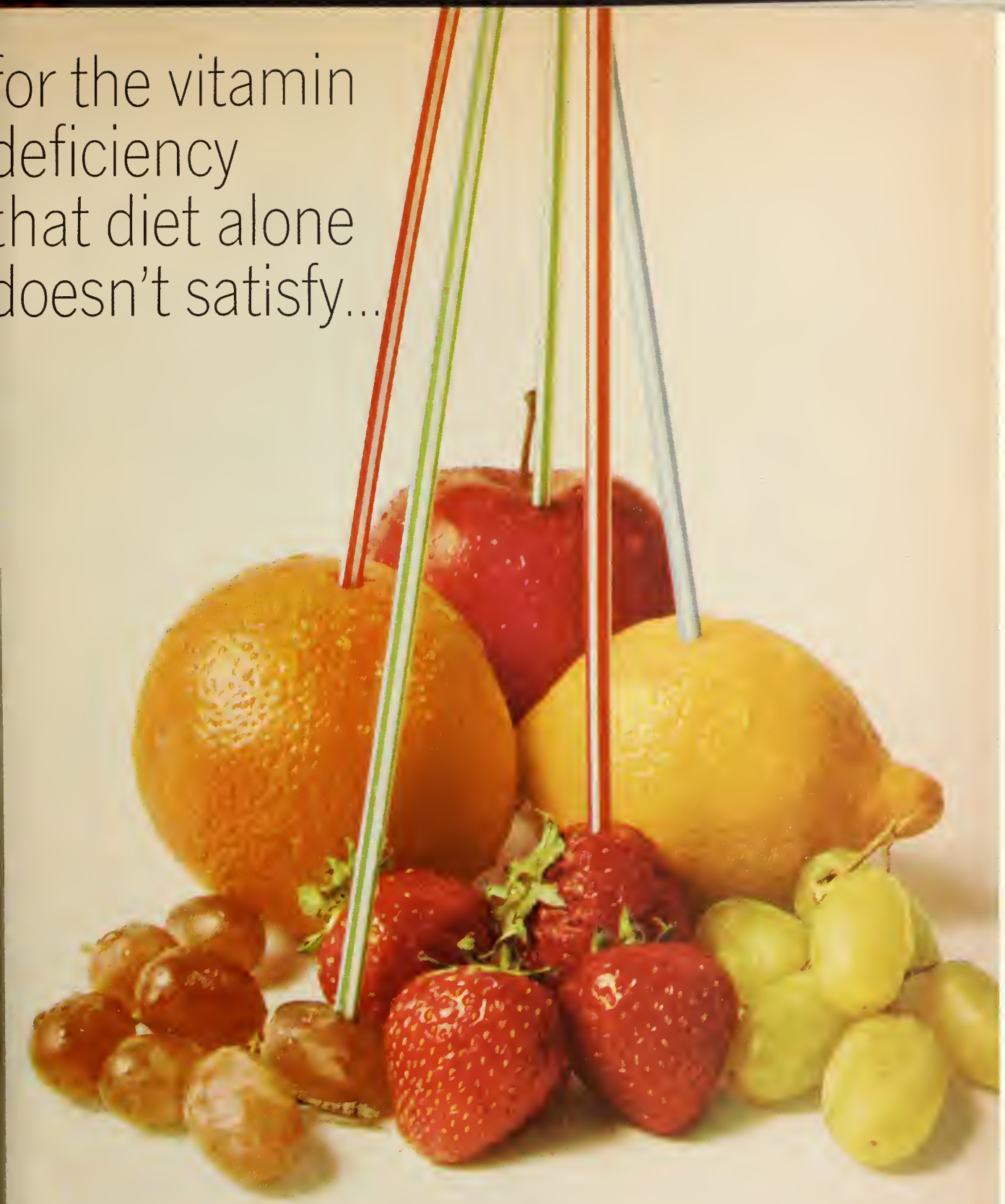

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Volume Sixty-one | Brunswick, Maine, February 1970 | Number 2

The Organization of Rural Health Services

An Approach by the Upper Kennebec Valley Regional Health Agency

RICHARD T. CHAMBERLIN, M.D.

INTRODUCTION

There is a great deal of talk these days about the health care system. Depending from which vantage point one views it, the system – or non system as it has also been called – is considered excellent, such as the great strides made in the capability of modern technology to improve health – or terrible, such as the poor distribution of these new technologies to all people.

This should not be too surprising if one takes the physician's traditional approach to a medical problem and uses the case method of study applying it to the health care system. I should like, therefore, to begin by presenting a case history briefly which serves to illustrate the complexities of the problem of providing health care to a real patient and then by analogy describe one approach used to solve some of these problems in a region by the means of a community health agency. Just as the patient's problems are difficult to solve – so are the community's.

CASE PRESENTATION

A sixty-three-year-old woman was admitted to the hospital on 12/5/68 and discharged on 9/13/69. The new acute problems in this patient's life secondary to the trauma of an automobile accident were as follows:

1. An open wound of the right knee with a compound and comminuted fracture of the patella with interuption of the quadriceps mechanism.
2. A closed badly comminuted and displaced fracture of the left distal femur.
3. An extremely comminuted fracture of the left os calcis.
4. Several minor fractures of the right foot.
5. A severe chest contusion, the pain of which mimiced that of an acute coronary occlusion.
6. Multiple contusions and abrasions.

When the dust had settled from the initial care of these acute problems and the complete history was obtained, one was able to identify several old established and stable medical problems which had existed in this patient's general medical situation:

1. Extreme obesity – over 300 pounds.
2. Disabling athritis to the point of forcing the patient to be ambulatory only with the help of a walker.
3. Probably a severe depressive reaction. There was no formal psychiatric consultation but symptoms were suggestive that a significant depression had existed in this patient's life for some time.

Added to this background were complications which occurred in the hospital:

1. Acute gangrenous cholecystitis followed by a cholecystostomy and drainage on the thirty-second hospital day.
2. An acute febrile reaction, probably secondary to genitourinary tract infection, causing a delay in her convalescence.
3. An acute bursitis which also interfered with the patient's progress in her rehabilitation program.

One can review this case in many ways – one of which might be to consider it from the standpoint of the personnel involved in her total care. These are not necessarily listed below in the order of their involvement in her case nor of their importance, but nevertheless all were involved.

A. Personnel at the scene of the accident
   1. Police.
   2. Bystanders.
   3. Firemen.
   4. Wrecking Crew.
   5. Ambulance Personnel.
   6. Physicians – In this case one was called to the scene of the accident.

At this point, we must ask ourselves several questions. Are these personnel all trained in appropriate emergency medical treatment necessary to save lives and prevent additional trauma to the injured? Whose responsibility is it to provide such training and keep it updated? Are the latest techniques of extrication available? Who is to provide this equipment, maintain it, and train people to use it properly? Are adequate communications from the scene to the hospital available? Are they used? Who is to purchase that equipment? Who is to see that all emergency personnel are on the same radio wave lengths? Are the ambulances properly equipped? Whose responsibility is it to see that all of this phase of emergency care is coordinated for the most rapid, efficient, and safe functioning? Is it the city or town government? Is it the hospitals? Is it the physicians?

B. The Emergency Hospital Aspect

1. Emergency Room personnel.
2. The physician on call.
3. Consultants on call, in this case orthopedic and medical.
4. Services on call – Laboratory, x-Ray Operating Room, Anesthesia.
5. Intensive Care Unit personnel.

Again more questions arise. Even if the organization at the scene is proper and efficient much might be lost if the hospital emergency care plan is inadequate. Whether it be for one patient or ten patients as in a disaster plan, the principle is the same. Should hospitals have full-time highly trained personnel in Emergency Rooms twenty-four hours a day – seven days a week? Should they be doctors, and if so should they be Emergency Room specialists? Should they be trained emergency technicians? If so, whose responsibility is it to set standards for their training and certification? Where do they stand in relation to other traditional medical personnel in the wage structure?

C. The Sub-Acute Phase

1. Social Service – In this case the patient was already on a State Aid program and the Social Service Department automatically were notified of the patient's admission and became involved to see that the proper information, forms, etc. were initiated. This occurred in this case while the patient was still in the Intensive Care Unit.
2. Acute Medical-Surgical Floor Personnel after transfer out of Intensive Care Unit.
3. General Surgeon at the time of the acute cholecystitis.

Still more questions. With rising hospital costs and with acute services often the most expensive on a per diem basis, whose responsibility is it to oversee the proper utilization of these services? What criteria can be developed to help determine and document the need for the levels of care for every patient – particularly the acute phases?

D. The Rehabilitative Phase

1. Dietitian – In this case, especially due to the gross obesity, a carefully planned dietary therapy program was necessary to provide weight loss and yet to provide proper protein nutrients needed for wound healing, bone healing, etc.
2. Physiotherapist.
3. Prosthetic Supplies – Crutches, walkers, orthopedic shoes.
4. Dentist. In this particular patient, as she lost weight her dentures did not fit any longer and then, with the difficulty in chewing food, she found it difficult to stay on her rigid diet. New dentures were needed.
5. Voluntary Service Organizations. Since the state programs do not furnish such things as dentures and the patient had no funds, a voluntary service club was contacted and did provide funds for the purpose of purchasing her dentures and providing dental services.
6. Regional Home Health Services.
7. Follow-up Care – In this case an out-patient department clinic.

Obviously more pertinent questions arise. How will all of these more chronic services be coordinated so that the least amount of time and expense will be involved? Who is responsible? Is it necessary for a physician personally to supervise every single step along the way? Who is to train these personnel and keep them at acceptable levels of functioning? Can one really separate any of these personnel and/or services from the entire picture and claim that it is not the responsibility of the medical profession in the total care of this patient?

As I have pointed out above, this case is being used simply to demonstrate the complexities of the total medical problem as it applies to a single case. Is it any wonder then that the entire medical care system is also difficult to study and evaluate, and is it any wonder that it is difficult to provide the means to improve it? To solve these problems one must start somewhere in the continuum of medical care. In the experience to be described below, the entree was via the problem of home health services. This health care problem can also be presented as a case history.

THE CASE OF HOME HEALTH SERVICES:

CHIEF COMPLAINT: Lack of adequate home nursing services.

PRESENT ILLNESS: This one hundred and sixty-year-old community in Central Maine found itself lacking in adequate services in 1966. The problem was a chronic one and medical consultants, Drs. Smillie and Curran, reported in 1956 that the lack of organized health care services to patients in their homes was one of the major unmet needs in the medical care of the State of Maine.[1] One attempt had been made to rectify the problem by the involvement of an interested group of citizens and physicians on a Health Services Committee in early 1961. This committee was instrumental in effecting the decision of the city to hire a city nurse whose duties were to provide both public health nursing to the city as well as home health nursing to patients discharged from the local hospitals. Although this helped to ease the pain temporarily, the nurse had no direct medical supervision and some of the problems continued to exist. In addition, her public health duties frequently interfered with her abilities to provide all of the needs of home health nursing. One of the community's hospitals, the Thayer Hospital, attempted to develop a homemaker service to ease the burden on the nurse and provide a wider range of home services. Although this was initially successful, the program failed when the hospital turned the administration of the program over to another existing health agency in the community. Other attempts to alleviate the situation failed when Community Chest Programs were too limited and the Red Cross organization could not fill the void. Applications to private foundations for assistance also failed to produce a cure.

PAST HISTORY: The community initially involved had developed a number of traditional medical resources with two allopathic and one osteopathic hospitals, the Seton Hospital, the Thayer Hospital, and the Waterville Osteopathic Hospital. In all, there was a total of about fifty allopathic physicians and about fifteen osteopathic physicians representing a wide range of specialty services. There had also developed the usual number of traditional interpersonal and interinstitutional jealousies, suspicions and rivalries all as a result of two chronic diseases called "poor communication" and "lack of understanding." The latter disease had spread to adjacent communities and areas who were also partially disabled by good old Yankee conservatism.

FAMILY HISTORY: The disease, lack of home health services, was a familial affair existing in all surrounding communities to one degree or another. Many of these brother and sister communities were suffering from a general lack of resources as well.

SOCIAL HISTORY: The community had recently been exposed to a national epidemic of a virus which went by the experimental designation of PL89-97 (Medicare) with its strains XVIII and XIX and there were hints of further new waves approaching called PL89-239 (Regional Medical Program) and PL89-749 (Comprehensive Health Planning). Much advice and attitudes seemed to be that "you can't lick em so you might as well join em."

REVIEW OF SYSTEMS: This was generally non contributory except for a condition known as general lack of funds.

PHYSICAL EXAMINATION: The total body (region) involved has a fairly well developed and well nourished area (community) at its hub, but extends in such a way as to encompass approximately four thousand square miles and a population of approximately eighty to eighty-five thousand people. It includes one whole county and parts of two other counties with ten hospitals ranging from a size of fourteen beds to one hundred and sixty beds.

The Head: The community initially feeling the lack of home health services is an area consisting of one city and three towns with three hospitals totalling about three hundred and forty beds with approximately fifty allopathic and fifteen osteopathic physicians representing virtually all of the medical specialties and specialty services.

The Trunk: The head is connected via the central trunk of the Kennebec River Valley and its main transportation route U.S. 201 to its most distal parts some ninety to one hundred miles away where there are located other small hospitals of fourteen and twenty-two beds respectively with medical staff as small as one and three physicians respectively.

The Economics: The State of Maine in general and the area described above in particular has a lower per capita income than the nation as a whole on the average.[2]

The People: The average age of the population in the State of Maine in general and in the area described above is older than that of the country as a whole.

Medical Coverage: The state as a whole has had a loss of physicians since the turn of the century and outside the urban areas in the area described above the ratio of physicians to population falls to as small as one to ten thousand in the more remote rural areas.[3]

IMPRESSION: The need for action.

TREATMENT: The treatment consisted of several different aspects as listed below:

A. The Demonstration of Need
   1. Through the efforts of the Department of Rehabilitation and Long-Term Care in Thayer Hospital, the need for out-of-hospital services, particularly home health nursing, was documented in the immediate more urban area.[5]
   2. Through the efforts of the Bingham Associates Fund, the documentation of this need in the more rural areas was also accomplished by some extensive and tireless field work which was done by the former field director of the Bingham Associates Fund in Maine, Mr. George Nilson. This identified not only the needs, but also some of the difficulties which might become barriers to the implementation of programs to fill these needs. These barriers were usually built on old established traditions.
   3. These two efforts were studied and summarized by an outside planning consultant, Dr. Wilson Smillie, in early 1966.

B. Cooperative Involvement
   1. A planning Board of Directors consisting of representatives of the three hospitals in Waterville, the Seton Hospital, the Waterville Osteopathic Hospital and the Thayer hospital was formed with additional representation from the city government and other interested citizens. These individuals donated considerable personal time to this effort. This Board of Directors kept close liaison with committees and organizations on the state level.
   2. The Waterville hospitals also demonstrated tangible support of the project by diverting their share of Community Chest funds to the Board of Directors as a partial funding of the early phases of the project.
   3. The State Department of Health and Welfare supported the project with whatever funds were available to it for such planning purposes at that time.
   4. A physician Advisory Group to the Board of Directors was formed to help establish medical policies for the Home Health Service.

C. Interim Experimentation with Federal Funding
   1. With the advent of Medicare certification requirements, the overall project scope perhaps gained new dimensions. An Interim Home Health Agency was formed using the expertise of those members of the home health care team as already existed and were already functioning in the Thayer Hospital Department of Chronic Care and Rehabilitation. This interim project was designed to study the feasibility of a home health agency as well as to become certified by the Social Security Administration as an official agency thereby becoming eligible to be reimbursed for services rendered to Medicare patients.

D. Joining of Service with Planning for Service
   1. As experience with home health nursing grew out of this small scale operation, various consultants to and principals of the program began to envision how this initially cooperative venture might serve as a potential model for future involvement in regional planning for all health services in general and not simply home health nursing. With the development of public law 89-239, Regional Medical Programs, and public law 89-749, Comprehensive Health Planning, on the national scene and the atmosphere of involvement and cooperation already developing on the local scene an administrative structure was developed for what had been the Interim Home Health Agency. This new venture became incorporated as the Upper Kennebec Valley Regional Health Agency and was developed in such a way that would allow for it to continue to provide home health services as well as to provide comprehensive health planning for the wide range of health needs as they became visualized within the entire region.

E. Funding from Regional Medical Programs
   1. A grant request embodying these principles was submitted to Maine's Regional Medical Program in early 1968 and was approved and funded in July of 1968. These funds supported various divisions of the Upper Kennebec Valley Regional Health Agency such as the core staff, the Division of Continuing Education, the Regional Blood Bank Service, as well as for providing funds for development of communications and transportation and for the training of allied health personnel. Much of the funding involved was on a decreasing basis over a period of three to four years with the expectation that some of these divisions would become self-sustaining. Since Regional Medical Program funds cannot be used for direct patient services, the Home Health Division specifically was excluded from this funding mechanism. Its funds continued to be derived from Community Chest plus reimbursement for services to Medicare and Medicaid patients.

F. Certification as a 314 B Agency of Public Law 89-749 Comprehensive Health Planning
   1. Presently, a grant application has been submitted to the State's 314 A Agency and the Public Health Service for recognition as a comprehensive health planning agency for the Upper Kennebec Valley Region of Maine. It is believed that the agency structure is such that it may serve as a model demonstration of how Regional Medical Programs and Comprehensive Health Planning can co-exist and each help to solve the many problems of the health care system.

PROGNOSIS: The course of treatment is still in its early phases. The initial response to treatment has been satisfactory. With the formalization of the planning function, both within the Upper Kennebec Valley Regional Health Agency itself and on the State level, we are confident that this approach to planning for service while actually rendering these same services under the guidance of a single agency will be successful to curing some of the ills of the health care system in the future.

REFERENCES

1. The Unmet Needs in Medical Care of Rural People – The

Continued on Page 32

Hyperphenylalanemia

Incidence in Maine Since 1964

EDMUND N. ERVIN, M.D.*

Since January 1964, a newborn testing program for phenylketonuria has been in effect in the State of Maine. In 1965, the Legislature passed an "Act Relating to Testing of Newborn Infants for Detection of Causes of Mental Retardation." This legislation required "hospitals, maternity homes, and other maternity services to test or cause to be tested newborn infants for the presence of metabolic abnormalities which may be expected to result in subsequent mental deficiencies." The first of such metabolic abnormalities for which a testing program was set up is phenylketonuria.

The condition is an autosomal recessively inherited defect of a metabolic enzyme which converts phenylalanine to tyrosine. Mental retardation is the most striking clinical feature of the untreated case. The exact nature of the biochemical changes which produce the brain damage is not known, but early dietary treatment is effective.

In 1953, Bickel, Gerrard and Hickemans[1] prepared a special protein hydrolysate low in phenylalanine content. When the child with phenylketonuria was fed such a diet, the plasma phenylalanine was reduced and the phenylpyruvic acid disappeared from the urine. In 1959, he reviewed his experiences[2] at the First International Medical Conference on Mental Retardation in Portland, Maine. Detection of the condition in the first weeks of life and institution of dietary treatment to prevent the brain damage which results in mental retardation is the objective of the program. Guthrie[3] proposed a method for the mass screening of populations and it is this test which is used in the State Diagnostic Laboratory of Dr. Charles Okey on the newborn blood samples taken in nurseries throughout the whole State.

This appeared to be a simple and effective solution of a distressing problem. However, with the widespread use of newborn screening programs, an increasing number of patients with elevated blood phenylalanine levels were being detected. The incidence of classical phenylketonuria in the population had been estimated to be about 1 in 20,000 before the introduction of the Guthrie screening assay but the increased numbers of reported hyperphenylalanemias prompted a revision in the estimate to 1 in 10,000.

The middle nineteen sixties was a confusing period as criteria for detection and treatment of this condition were evolving. MacCready[4] reported on the Massachusetts experience and mentions several cases in which no confirmation of the elevated phenylalanine was made apart from the Guthrie test. An elevated blood phenylalanine does not make the diagnosis of phenylketonuria. Yet, this was happening all over the country and infants were being placed on low phenylalanine diets on the basis of a positive Guthrie test alone. The dietary regulation was not always simple but fraught with some danger if the level of blood phenylalanine was kept too low. Then reports began to appear of children developing a phenylalanine deficiency syndrome who were found never to have had phenylketonuria or even hyperphenylalanemia. The problem was becoming more complex. What has been our experience in the State of Maine?

Since January 1964, there have been fourteen infants with hyperphenylalanemia detected in the newborn screening program using the Guthrie method. Eight infants or 57% were subsequently proven to have the classical form of phenylketonuria. Definitive diagnosis of the condition remains a problem. Some of the causes of hyperphenylalanemia require no treatment, eventually achieve normal blood levels of phenylalanine, and do not produce the end results of severe mental retardation seen in the untreated case of PKU. Because the treatment is hazardous as well as costly and difficult to manage, it is imperative that a definitive diagnosis is made.

In a review article on Hyperphenylalanemia in the May 1968 volume of *Pediatric Clinics of North America*[5], Carpenter, Auerbach, and DiGeorge discuss the pathways of phenylalanine metabolism. They state that the main catabolic route is via hydroxylation to tyrosine for which two distinct enzymes (phenylalanine hydroxylase and dihydropteridine reductase) are required and a ubiquitous cofactor. A complete block in the conversion of phenylalanine to tyrosine leads to classical PKU. Tyrosine is further metabolized by tyrosine transaminase to phenylhydroxyphenylpyruvic acid which in turn requires the enzyme phenylhydroxyphenylpyruvic acid oxidase for conversion to homogentisic acid and eventual oxidation to CO_2 and water. They define a minor route of phenylalanine catabolism by way of transamination (phenylalanine transaminase) to phenylpyruvic acid and subsequent conversion to phenyllactic acid, phenylacetic acid, and orthohydroxy phenylacetic acid. Some phenylalanine is not completely oxidized but is converted to metabolities such as epinephrine, melanine and thyropine via tyrosine. They point out that impairment of any of these pathways could lead to the accumulation of phenylalanine.

Therefore hyperphenylalanemias have been classified as:

1. Classical PKU.

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a. rapid rise in blood phenylalanine levels in the first weeks of life (over 30 mg. percent).
b. phenylpyruvic acid and its catabolites can be detected in the urine.
c. these biochemical abnormalities remain unchanged throughout life.
d. phenylalanine tolerance is low.
e. if untreated it results in mental retardation.

2. Atypical PKU.
These cases represent a varied group hitherto unrecognized when the diagnosis depended on the detection of phenylpyruvic acid alone in the urine. Only since the newborn screening procedures of blood levels have investigators become aware of other metabolic possibilities which are explained by genetic mutations or perhaps polygenic factors. Many show varying blood levels rarely exceeding 20 mg. percent. Phenylpyruvic acid may or may not be present in the urine. Finally, there is variability in the incidence of mental retardation. Varying responses to phenylalanine loading tests.

3. Phenylalanine Transaminase Deficiency.
a. hyperphenylalanemia manifested only during high protein feeding or phenylalanine loading otherwise feedings with formulas of normal protein content resulted in normal phenylalanine levels.
b. low – absent urinary pyruvic acid.

4. Delayed Enzyme Maturation.
a. phenylalanine levels usually below 20 mg. percent.
b. blood tyrosine is elevated more markedly than phenylalanine.
c. phenylpyruvic acid in the urine.
d. most frequently seen in premature infants.
e. phenylalanine elevation is transient; tyrosine elevation may persist for several months.
f. phenylalanine loading tests are normal when blood levels have returned to normal.

5. Transient Hyperphenylalanemia.
a. phenylalanine levels are usually below 8 mg. percent and return to normal within a few weeks.
b. tyrosine levels are normal.
c. subsequent phenylalanine loading tests are normal.

From January 1964 to October 1969, 92,237 infants have been screened and a total of 14 infants were noted to have elevated blood levels. While all infants detected in the screening program have not been studied in the same manner, we can attempt to classify them according to the various types of hyperphenylalanemia.

Type I	Phenylketonuria	8
Type II	Atypical phenylketonuria	1
Type III	Phenylalanine Transminase Deficiency	
Type IV	Delayed Enzyme Maturation	2
Type V	Transient Hyperphenylalanemia	2
	* (One infant is still being studied but the data suggests that he is a heterozygote.)	1*

The infant with classical PKU requires prompt institution of diet therapy with continuing follow-up and supervision. Such management necessitates frequent monitoring of blood phenylalanine levels (ideally 6-10 mg. percent) and close liaison between the responsible physician and the nutrition consultant for readjustment of the diet. Too restrictive a diet in the classical PKU as well as institution of the diet in an infant with hyperphenylalanemia due to other causes may result in a phenylalanine deficiency syndrome[6] characterized by listlessness, failure to gain weight, eczematous rash, hypoglycemia, anemia (iron deficiency and megaloblastic) and osteoporosis.

A rapid rise of blood phenylalanine to levels above 30 mg. percent is no diagnostic problem, but the infant with levels below this figure will need weekly monitoring of blood levels of phenylalanine and urinary excretion of phenylpyruvic acid. If the blood level of phenylalanine remains below 20 mg. percent and phenylpyruvic acid is not demonstrated or only slightly in the urine, the diagnosis is difficult. Continued weekly monitoring of blood phenylalanine levels is imperative.

One must confirm the presence of hyperphenylalanemia by a chemical method in all those infants who show a blood phenylalanine level in excess of 4 mg. percent by the Guthrie method. (Blood levels are somewhat higher by this method than by chromatography or fluorometric determination.) At the same time, the blood level of tryosine is determined to rule out a delayed maturation of this enzyme system. If the hyperphenylalanemia is due to delayed maturation of tyrosine oxidation, then the blood level of tyrosine will be higher than of phenylalanine.

With these principles in mind, routine monitoring of blood phenylalanine levels, etc., has allowed us to classify with some certainty all but 2 of the 14 infants first detected. Eight of this group have classical PKU and are under dietary management with good chemical control and no evidence of mental retardation. Four of these infants (2 premature infants with delayed enzyme maturation and 2 infants with transient hyperphenylalanemia) have been followed for over two years and no longer demonstrate elevated blood phenylalanine levels.

One of the remaining two infants is presumed to be a case of atypical PKU. She was born 3/24/69 weighing 7 lbs., 3 oz., after a normal full term pregnancy and delivery. Neonatal blood phenylalanine was reported as normal but when repeated at six weeks of age, it was 20 mg. percent. Repeated levels by the Guthrie method varied from 13 – 20 mg. percent. Chemical determination of blood levels in June 1969 revealed phenylalanine 14.0 mg. percent and tyrosine 1.6 mg. percent. She was being fed a somewhat lowered protein intake. Subsequent Guthrie assays revealed phenylalanine levels of 14.0, 18.0, and 20 mg. percent. Growth and development were normal in all aspects. It was reported that repeated urine testing with Phenistix® was negative.

Because the blood phenylalanine levels were approaching the level of 20 mg. percent, it was decided to admit the patient for study. A tolerance test, using 630 mg. of L-phenylalanine revealed a fasting level of 13.8 mg. percent, ½ hr. 37.5 mg. percent, 1 hr. 44.5 mg. percent, 2 hrs. 62.5 mg. percent and 4 hrs. 69.9 mg. percent. The rapid rise and the sustained height are significant and typical of classical PKU. However, the tyrosine levels at the same time revealed a fasting level of .87 mg. percent, ½ hr. 2.5 mg. percent, 1 hr. 1.7 mg. percent, 2 hrs. 1.7 mg. percent, and 4 hrs. 5.9 mg. percent. Urine was positive in all instances for abnormal metabolites and revealed the presence of 20 mg. percent orthohydroxyphenylacetic acid.

This case probably represents one of atypical PKU. Obviously, some enzyme or enzymes are present though in limited quantity as evidence by conversion of some phenylalanine to tyrosine yet insufficient to maintain a fasting level of phenylalanine within the normal range. Frequent monitoring of her blood levels will continue but no diet, other than one of lowered protein intake, will be instituted unless her phenylalanine levels by chemical determination are in excess of 20 mg. percent and there is a change in her clinical status.

The other infant, born April 1969, is currently being studied. Despite the fact that the initial blood levels never rose above 4 mg. percent, the infant was placed on Lofenalac® for eight weeks which could have had tragic consequences. These studies were initiated to confirm the diagnosis and to justify continuation of the diet.

A tolerance test using comparable amounts of L-phenylalanine revealed a fasting level of 1.86 mg. percent, ½ hr. 3.31 mg. percent, 1 hr. 10.66 mg. percent, 2 hrs. 9.63 mg. percent, and 4 hrs. 8.72 mg. percent. However, he did not raise his plasma tyrosine level; a fasting level of 1.38 mg. percent, ½ hr. 1.15 mg. percent, 1 hr. 0.78 mg. percent, 3 hrs. 0.68 mg. percent, and 4 hrs. 8.72 mg. percent. No orthohydroxyphenylacetic acid could be found in the urine. These findings demonstrate a decreased ability to metabolize phenylalanine and suggest heterozygosity for the condition. In other words, the diminution of phenylalanine hydroxylase activity might be the effect of one abnormal gene. It also suggests that the increased levels of phenylalanine depressed his plasma tyrosine levels. Further studies are contemplated to include observations on a normal diet and liver biopsy for enzyme content. Testing for possible heterozygotes is an aid in genetic counselling and in this case has been an additional check for an asymptomatic infant erroneously thought to have phenylketonuria and placed on a low-phenylalanine diet.

ACKNOWLEDGMENT

The author is indebted to Dr. Ellen Kang, Children's Medical Center, Boston, Massachusetts, for chemical determinations and critical comments.

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Heterotopic Pulmonary Ossification

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INTRODUCTION

Idiopathic pulmonary ossification has been described in several cardiac and primary pulmonary diseases. Most of the cases described are of the nodular type which is seen almost exclusively in association with mitral stenosis. A diffuse, branching type has been described in elderly people in association with senile alterations in perivascular connective tissues. The purpose of this paper is to describe a case of severe pulmonary ossification in association with congestive heart failure secondary to coronary heart disease or an ill-defined myocardiopathy with associated pulmonary insufficiency consistent with massive left pulmonary embolus.

CASE PRESENTATION

This 55-year-old diabetic male was first seen at the Thayer Hospital in May 1968, for generalized weakness. His past history consisted of myocardial infarctions in September 1967, and in February 1968, with associated congestive heart failure. His diabetes was of mature onset and had been controlled with oral hypoglycemic agents. His occupation had been that of a laborer in a shoe factory prior to his incapacitation with his first myocardial infarction in 1967. There had been no exposure to excessive amounts of dust and his travels had been limited to New England. Laboratory data at that time revealed modestly elevated triglycerides, uric acid and glucose. A chest roentgenogram showed a normal heart size and clear lung fields. An EKG showed left axis deviation with superior intraventricular block and S-T and T wave changes consistent with superior lateral ischemia.

He was then lost to follow up until May 1969, when he presented in severe congestive heart failure. On physical examination, his blood pressure was 120/80, pulse 120 and regular and respirations 30. The neck veins were engorged, an S_3 and S_4 gallop was noted, but no cardiac murmurs could be heard. The liver was moderately enlarged and the lower extremities showed a 2+ pitting edema. Very mild cyanosis of the nail beds was noted, but there was no clubbing.

Laboratory data showed a proteinuria of 450 mg %, but the urine was otherwise normal. Hemoglobin was 16 gm with a normal white count and distribution. The electrolytes were normal as were the sedimentation rate, thyroid function, creatinine, ASO titer, calcium, phosphorus and alkaline phosphatase. Total protein, A/G ration and serum electrophoresis were also normal. Skin tests for tuberculosis and fungi were negative. L. E. studies were negative. Blood cultures showed no growth after ten days. EKG showed sinus tachycardia, lateral wall ischemia and a probable old anterior infarction. Pulmonary function studies revealed good ventilatory capacity with a vital capacity of 3200 cc, or 78% of predicted value. Arteriolar blood gases while the patient was breathing room air was ph 7.52, $PaCO_2$ 34.5, PaO_2 58. The PaO_2 increased to 160 mm while the patient was breathing 100% O_2. Lung scan showed almost complete failure of visualization of the left lung and normal uptake by the right lung.

The patient was anticoagulated and symptomatically treated for congestive heart failure. He was discharged to his home after three weeks with modest improvement in his clinical status.

One month later, he was readmitted to the hospital in severe congestive heart failure. The physical examination and laboratory data were essentially unchanged. The usual regimen for treatment of congestive heart failure was initiated, but again with minimal improvement in his clinical condition. A chest roentgenogram showed greater diffuse infiltration of the left lung compared to the previous examination several months earlier. A repeat lung scan was essentially unchanged. Pulmonary angiograms were obtained during an injection of 40 cc Conray® 60 in the main pulmonary artery with a Cordis injector. This study revealed a normal right arterial distribution and delayed filling of the left main pulmonary artery and markedly decreased peripheral filling throughout the left lung. The findings were consistent with partial vascular occlusion.

In view of findings that seemingly indicated a non-resolving large pulmonary embolus, thoracotomy and exploration of the left pulmonary artery was believed to be indicated. After consultation, the patient was brought to surgery for pulmonary arteriotomy and lung biopsy. At surgery, the main pulmonary artery was incised and was found to have a perfectly smooth intima. There was no evidence of intra or extraluminal occlusion. The secondary branches were also inspected, but no evidence of thrombosis could be detected. Inspection of the lung, however, revealed diffuse, hard nodules throughout, especially profuse in the upper portion of the lower lobe. Exploration of the right chest was not carried out.

The lung biopsy showed a diffuse interstitial fibrosis with thickening of the alveolar walls, cuboidal metaplasia of the alveolar endothelium and masses of heterotopic bone showing well defined osteoblasts and deposition of cement substance in a mosaic pattern. The bone formation appeared to be within the pre-existing small blood vessels. The alveoli contained hemosiderin laden macrophages.

Postoperatively the patient's clinical status remained unchanged and he was subsequently discharged to his home on bed rest, digitalis and an extensive diuretic regimen. Cardiac catheterization was recommended to assess the individual pulmonary resistances, but the patient refused.

DISCUSSION

Dystrophic calcification is not infrequently seen in tuberculosis, histoplasmosis and other chronic lung diseases. The process is due presumably to the deposition of lime salts in necrotic tissues. This hypothesis was suggested by Wells[5] who noted the tendency of calcium to deposit in the lungs, stomach and kidneys which are organs that excrete acids in the presence of relative cellular alkalinity. He also noted that a reduction in carbon dioxide causes certain metabolic changes, which in the presence of relative alkalinity, results in deposition of calcium compounds. He concluded that these metabolic alterations in the acid-base relationship were most important in the precipitation of calcium in normal tissues. It is interesting to note that calcification may occur in normal tissues and that it is a function of metabolic and/or electrolyte disturbances, at present poorly understood. There is general agreement, however, that calcification of the lungs does not undergo ossification. Soter[4] has described a case in which both conditions were present, i.e., ossification and calcification, but concluded that these coexisted by chance and that predispos-

Fig. 1
Lung scan showing almost complete avascular pattern of the left lung.

Fig. 2
Chest x-ray of May 1968, interpreted as being essentially normal.

Fig. 3
Chest x-ray of July 1969, showing nottling of the left lung field.

Fig. 4
Pulmonary angiogram showing delayed filling of the left main pulmonary artery and markedly decreased peripheral filling.

ing factors for both conditions were present. The major predisposing factor for calcinosis, as we have described, is the metabolic alterations associated with relative alkalinity of tissues. The major predisposing factor for ossification appears to be chronic pulmonary congestion, and although this is not generally agreed upon, congestion appears to be present in most of the reported cases. However, since ossification is not seen in the usual picture of congestive heart disease, other etiologic factors must be present. Various hypotheses have been pro-

posed, but none seem to offer an adequate explanation. Some of these theories are as follows: (1.) Bone nodule formation as a late complication of rheumatic pneumonia; (2.) Reorganization of hemosiderin deposits with subsequent ossification; (3.) Pulmonary hypertension with associated pulmonary edema and ossification of the fibrinous exudate; (4.) Transformation of mesenchymal cells which are generally attached to capillary surfaces; (5.) Thrombosis of septal capillaries; and (6.) interstitial pneumonitis.

The present case offers several points of diagnostic and therapeutic interest. The clinical picture is that of congestive heart failure secondary to coronary heart disease with a past history of myocardial infarctions. However, review of previous EKG's failed to show definite evidence of infarction and unfortunately the records were not available for perusal. It may well be that the patient had a poorly defined myocardiopathy. Laboratory data failed to explain the exact nature of this heart disease and myocardial biopsy for amyloidosis was not believed to be strongly indicated at time of surgery.

A chest roentgenogram obtained in 1968, one year prior to exploration, shows the lung fields to be entirely clear. However, a repeat chest roentgenogram one year later shows mottling over the left lung field. Soter[4] has described a case of probable psittacosis in which these ossified nodules developed within several months.

The findings by lung scan in our case were consistent with either extra or intraluminal vascular occlusion. Recent literature has stressed the inadequacies of lung scanning in attempting to establish the presence (or absence) of embolic phenomena. The presence of blebs, pneumonitis, or inadequate perfusion disorders offer diagnostic problems which can best be resolved by obtaining a thorough medical history and physical examination. The findings with pulmonary arteriogram and lung scans were comparable and although the reproduction of these arteriograms is somewhat poor, the avascular pattern of the left lung was evident. The patency of the pulmonary artery and the absence of extra or intraluminal disease in the primary and secondary left pulmonary artery branches were established at surgery.

From a physiologic point of view, some undefined factor associated with congestive heart failure would seem to have initiated ossification. However, the apparent unilateral aspect of this disease in our patient would indicate that the initiation of the disease was unilateral and, therefore, suggests that an interstitial pneumonitis may have been the precipitating factor. Ossification associated with calcified pulmonary thrombi are generally branch-like and more focal and limited than in the present case. The poor vascular filling during pulmonary angiography in the presence of patent pulmonary arteries would support the presence of unilateral pulmonary hypertension and clinically the presence of a large A-V shunt probably aggravates the underlying heart disease. Pulmonary resistances were not established since the patient refused cardiac catherization; however, a good case for left pneumonectomy could be made should contralateral resistances be normal.

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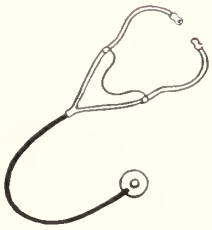

Cryosurgery With Special Emphasis on its Use in Ophthalmology

ROBERT J. TAKACH, M.D. and KEVIN HILL, M.D.

INTRODUCTION

Practical application of the principles of cryobiology has lead to the development of cryosurgery as a subspecialty which has broad application in medicine. Surgeons from "Neuro-" to "Uro-", from "Gyn." to "E.N.T." have used this modality in a wide variety of situations. Underlying this diversity of clinical application are a few fundamental attributes of low temperature which are summarized in Table I.

TABLE I

BASIC USES OF LOW TEMPERATURES IN MEDICINE

Use	*Examples*
1. Preservation of Tissue	a. Storage of blood, sperm and viable corneas b. Refractive keratoplasty
2. Destruction of Tissue	a. Pituitary ablation b. Cryothalamectomy c. Treatment of tumors (skin, eye, g.-u. tract, g.-i. tract, head and neck)
3. Production of Inflammatory Adhesive Response	a. Repair of retinal detachment b. Production of female sterility
4. Adherence of Cryo-instruments to Tissue	a. Cataract extraction b. Tonsillectomy c. Removal of cystic orbital tumors d. Removal of atherosclerotic cores from obstructed blood vessels

Appraisal of cryosurgical techniques suggests certain advantages over other methods of surgery. (1.) Dulling of sensory nerves by cold may permit the use of local, rather than general anesthesia. The pain which may develop after thawing of the tissues usually can be controlled by oral or intramuscular analgesics. (2.) Sharp delineation of the cryogenic lesion is particularly helpful in neurosurgery when destruction of discrete areas of neural tissue is required in the treatment of dyskinesias[1,2] and in otology when selective cryo-labryinthectomy is desired to relieve Meniere's disease.[3] (3.) Hemostasis during surgery is also advantageous although late bleeding may complicate the postoperative course.

NATURE OF THE CRYO-LESION

The effects of freezing temperatures upon tissues are complex and varied. Detailed discussion of them is beyond the scope of this presentation. Suffice it to say that freezing produces ice crystals in tissue. If the cooling is rapid, intracellular formation of delicate crystals results. Slow freezing produces extracellular formation of larger ice crystals which have more damaging effect upon the cell. This is partly due to mechanical disruption of the cell membrane and partly the result of tissue dehydration leading to denaturation of the lipoprotein elements of the cell membrane. Both intracellular and extracellular ice formation produce an abnormal increase in the concentration of electrolytes with consequent changes in pH which are also deleterious.

Electron microscopic studies have shown widespread changes in cell ultrastructure after freezing.[4] Some of these effects may be the direct result of freezing but, in tissues with a vascular supply, secondary damage may occur as a result of anoxia due to interruption of capillary circulation. In general, freezing will stop capillary and small vessel blood flow with relative sparing of large vessels. After thawing, blood flow may resume although the vessels will show definite microscopic changes and thrombosis may occur later.[5]

Another intriguing effect of freezing of tissue which has been established by animal experiments is the stimulation of autoantibody formation.[6] The evidence for this phenomenon occurring in humans is tenuous but

TABLE II

METHODS OF CREATING LOW TEMPERATURES
A. Change of State – conversion of a solid or a liquid to a gaseous state E.g. 1. "Dry ice" to carbon dioxide gas. 2. Liquid nitrogen or Freon to gas.
B. Gas Expansion E.g. 1. Compressed CO_2 2. Compressed N_2O
C. Thermo-electric Effect (Peltier principle) A direct current passing through the junction of two dissimilar metals causes the junction to get cold.
D. Magneto-junction phenomenon A thermo-electric junction placed in a magnetic field gets cold.

reports of remission of carcinoma after repeated freezing are suggestive.[7] Certainly the possibility of immunologic effects should be considered when cryo-lesions are produced in humans.

CRYO-INSTRUMENTATION

A great number of cryogenic instruments have been devised in the past few years. Despite this somewhat bewildering display of gadgetry, all instruments utilize one of a few methods of producing low temperature (Table II). The selection of an instrument by the cryosurgeon will depend primarily upon what tissues or diseases he is going to treat and, secondarily, the cost and maintenance of the instrument.

The instruments we have found most practical for our use in ophthlamic surgery are:

1. Small self contained units for cryoextraction of cataracts employing either the gas expansion principle (Bellows CO_2 unit) or the change of state principle (disposable liquid Freon unit). These units have found their greatest application in cataract surgery[8,9] but have also been useful in extracting blood clots from the anterior chamber.[10]
2. A more sophisticated instrument (Amoil's unit) which operates on the gas expansion principle.[11] This unit has the following capabilities:
   a. Temperature range control (-30 to -70 degrees C.).
   b. Ability to defrost the probe quickly.
   c. Ability to maintain a constant low temperature for prolonged periods.
   d. Ability to be applied to a tissue warm before freezing is initiated.

This versatility extends the range of usefulness of this instrument to include the treatment of retinal detachment, extraction of dislocated lenses, treatment of peripheral uveitis, herpetic keratitis, iris prolapse, and certain ocular tumors.

SPECIFIC USES OF CRYOSURGERY IN OPHTHALMOLOGY

Cataract

The removal of a cataractous lens from the eye by means of a cryo-probe has been shown to be safe and effective. A small metal probe (1-2 mm. in diameter) is cooled (-30 to -70 C.) by one of several available methods (Table II). The lens capsule and underlying cortex in the immediate area of the probe freeze and adhere to the metal lip. The lens can then be removed from behind the iris by careful traction.

Other methods (forceps, suction) are as effective as cryoextraction of the lens in most cases. However, there are special circumstances where the cryo-probe extraction offers advantages:

1. If the capsule (membranous covering) of the cataractous lens is particular weak and degenerated, the chance of removing the lens without breaking the capsule is much better. The ice ball formed involves both lens capsule and underlying lens tissue thus traction during removal is distributed more deeply into the lens and is less likely to tear the capsule.
2. If a lens dislocated back into the vitreous humor of the eye, a warm probe can be passed into the eye until contact with the lens is made. The cooling is initiated and the lens adheres and is extracted from the eye.
3. When the posterior surface of the cornea is diseased, it is desirable to avoid instrument contact with the cornea otherwise a marked progression of the disease process is very likely following the cataract operation. The cryo-probe has made it technically possible to slide the lens out from beneath the cornea with minimal or no contact of instruments or lens with the posterior corneal surface.

It must be emphasized, however, that cryoextraction does not replace other methods of lens removal. Rather, this method has its own range of usefulness as described above. It extends the surgeon's range of capability and thereby cuts down the overall complication rate in cataract surgery. Situations also exist where the methods of lens removal (forceps, suction) are definitely better than cryoextraction. For example, (a.) When a round pupil extraction is desired and the pupil dilates poorly. (b.) When the vitreous is fluid and removal of the cataract with lysis of zonules inferiorly but not superiorly is desired (to avoid losing the lens in the vitreous before it is grasped with the extracting instrument).[12] The important point is that these various methods of extraction (forceps, suction, cryoextraction) are complementary and the effective surgeon must know how to use each method in specific circumstances.

Retinal Detachment

To cure a retinal detachment, the retinal hole or holes must be sealed off by producing an adhesive chorioretinitis. During the procedure, the detached retina must be brought into contact with the irritated, "sticky" choroid-

TABLE III

COMPARISON OF RESPONSE OF OCULAR TISSUES TO HEAT AND COLD

Cold (Cryotherapy)	*Heat (Diathermy)*
1. No destructive effect on scleral tissue.	1. Causes scleral necrosis
2. No scleral shrinkage	2. Causes sclera to shrink
3. Does not injure large ciliary nerves or vessels on direct application	3. Causes destruction of cilary nerves and vessels if applied directly to them.
4. May affect vitreous but only with intense application	4. Moderate application causes alteration of vitreous

sclera layer. Either heat (diathermy) or cold (cryotherapy) will injure the choroid enough to cause the scarring. Although both modalities produce chorioretinal scarring, there are certain differences in the response of the ocular tissues to heat and cold. (Table III).

Because of these differences, the retinal detachment operation in many cases can be performed with less trauma to the eye by using cold as the irritative agent. The treatment of retinal detachments using cryo-applications to produce chorioretinal scarring has been used extensively only in the past few years. There is considerable controversy over whether "cryo" or diathermy produces better results. In our cases, cryosurgery has produced results which are as good as those we have obtained using diathermy. Follow up of these cases, however, has not been as long as for those treated with diathermy. Both methods work well and have their particular applications. Cryosurgery is especially indicated where the sclera is very thin, and over holes in areas where large nerves and vessels are present. Certain holes far forward in the retina can be treated by cryo-applications directly through conjunctiva and sclera with no incision being necessary. This is a much less traumatic procedure than in the same type of case treated with diathermy which usually necessitates general anesthesia and dissection of conjunctiva and sclera.

Miscellaneous

Peripheral uveitis is an inflammatory reaction of unknown etiology of the posterior portion of the eye usually located inferiorly and behind the iris. It can be devastating to the eye over a long period of time and is very difficult to control. These eyes develop macular cystic changes with loss of central vision, hazy vitreous which also impairs vision, and secondary cataracts. Systemic steroids frequently are most helpful in controlling the inflammation but the side effects of the steroids used for many weeks or months may make it impossible to continue treatment. In some of these cases, the area of inflammatory exudate has been frozen repeatedly with the Amoil's unit. The rationale for this treatment is that the smaller vessels exuding inflammatory materials into the vitreous may be destroyed by repeated freezing. It is our clinical impression that in some of these cases vessel atrophy with subsidence of the inflammatory response has occurred after cryotherapy. This apparent therapeutic value of cold application is promising but must be substantiated by more clinical observation.

Other applications deserve mention. An *iris prolapse* can be treated by freezing the exposed iris thereby causing an atrophy of this tissue. *Herpes simplex keratitis* has been treated by destroying the involved corneal epithelium with cold application. The traction and temporary hemostatic effect of the freeze probe may be used when removing *iris tumors* or *cystic tumors* in or around the eye.

SUMMARY

Cryosurgery has become accepted as a useful part of the ophthalmic surgeon's armamentarium. Its full potential and conversely, its disadvantages have not yet been fully realized. The postoperative follow-up period of many cases is now becoming long enough to judge better its long-term effects and the results are encouraging. With time, there has been improvement of instrumentation with more reliable, smaller, easier to handle probes available. We will not abandon other proven surgical modalities but find that cryosurgery is a complementary and useful addition.

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Psychology of the Sick Bed

COR DEHART, M.D.*

INTRODUCTION

The general practitioner and the medical specialist will have to deal repeatedly with the question of psychological struggles and with what it means to be sick. The psychological struggles encountered by the person who becomes ill are many fold. It seems important to me to know more about the personality types of patients and to know more about the personality constellation in order to deal adequately with the psychological problems of being sick. As such, I have attempted to discuss some of the personality constellations and how these personality types will influence a sensible and reasonable approach in the patient-doctor relationship.

WHAT DOES IT MEAN TO BE SICK?

There have been interesting studies describing the pattern of expected behavior with certain obligations and privileges of being sick. Talcott Parsons[1] elaborates on the sick role in his book "The Social System." He says that, by being sick, there generally exists exemption from the performance of normal social obligations and there exists exemption from the responsibility of one's own state. The sick person has to live up to his obligations of being sick and by seeking and wanting to get better and by seeking medical help as soon as possible. The doctor then, in turn, has to verify and sanction the patients sick role. Variations in the sanctioning of privileges and obligations of the sick role are many and it depends on whether we are a woman or a man, whether we are a child or an adolescent or are of an older age, and it depends on our socio-economic status. We accept more easily the minor illnesses of a woman than of a man because of the notion that men should be very strong and tough. We also expect the sick person to get help and preferably medical help. If the patient does not want to get help, we frequently will doubt the legitimacy of the complaints. Frequently, when the patient has psychological problems, we assume that he is also responsible for his own condition and, as such, he has to make application for his treatment. If he does not seek treatment, we may doubt his legitimate right to exemption from normal life obligations. This patient may then risk the loss of his job, may risk close family relationships with his extended family, and may cause a conflict in his marriage. The patient has to pull himself together, otherwise the sympathy for the illness will wane and the persons around him may become more impatient and, at times, even angry. The neurotic person, especially, is not seen as sick and if the neurotic person is unable to perform his job, he may easily attract the angry feelings of his family or of the caretaking persons.

When the patient comes to the hospital, many more changes in his role will take place. The doctor-patient relationships will be changed. The patient cannot set up his own appointment, but will have to wait until the doctor makes his rounds. The patient may have to learn to associate with other moderately or seriously sick patients. The patient may have to adjust to certain hospital routines which are so vastly different from his own routine at home. He may have to subject himself to procedures foreign and threatening to him and he may have to deal with nurses, practical nurses and aides. In the meantime, the patient has much time to think and to ponder. The patient may have to lie passively in bed. He may ponder about his hope for betterment and improvement. He may doubt the outcome of his illness, may become suspicious about the procedures, about the tablets, the capsules and the injections given to him. His whole world shrinks to his sick room and he does not then belong to the working, to the playing, to the loving. He is tied to the physical well-being of his body. A time in the hospital is a time of confrontation with the frailties of his body and the finality of life. The illness may mean different things to the various personality types and personality configurations and, as such, the recognition of personality types in the patient dealing with his illness can be very helpful to the physician.

The following are several personality types which may be important to recognize:

THE OBSESSIVE COMPULSIVE PERSONALITY[2]

This person is easily recognized by the way he handles his anxiety. Usually this person is rather rigidly adhering to the standards of his conscience and he will do this in a ritualistic way. Certain order and routine has to prevail in his life. This person is quite neat and clean and punctual and may expect from others the same tidiness, punctuality and exactness. Oftentimes this person is rather obstinate and persistent. This orderly, controlled personality also relies heavily on thinking and planning and he is, therefore, unable to relax easily. When illness strikes the obsessive compulsive personality, his anxiety will increase and the rigidity of his personality structure may increase. This personality may ask questions about his treatment. He may want to know what is the matter with him, what kind of medication he is getting and he may want to know the exact schedule of his medications and may expect a doctor to come to see him about the same time each morning. Disturbances of any routine may increase his anxiety and, as such, in turn may increase his orderly, rigid ap-

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proach to control his anxiety. Usually it is well to go along with the defenses of the obsessive compulsive person. That is to say, to strengthen his defenses in making this hospital stay routine and explaining in detail what he will get for medication and which procedures will be undertaken. Active participation in decision making by the patient appears helpful. When the obsessive compulsive defenses break down, aggressive, hostile behavior and disorderly behavior may come to the foreground. When the patient undergoes anesthesia, he would like to have explained, in detail, what will happen. The explanation will frequently alleviate undue over excitement on the operating table or in the delivery room.

The Histrionic Personality

This personality may show considerable elaborate ways of attention seeking by either seductive or dramatic ways. His behavior pattern is characterized by easy excitability and emotional over reaction. The patient may be teasing or seducing in the relationship with the doctor. The patient loves to be noticed and to be listened to. Sometimes one may have the feeling that one is on the stage. The woman patient may be flirtatious and, by her deliberations, deny her anxiety about her illness. Rivalries may come into existence when the doctor pays more attention to the patient in the next bed. The way of controlling anxiety in this personality will be achieved by getting attention, admiration and sometimes total indifference toward illness (la belle indifférence). The doctor should be aware of the objective signs and symptoms of the illness and may have to reassure the patient despite the denial of any existence of illness. The doctor may have to shield against too great an involvement of a sexual nature, because the flirtatiousness was supposed to be a way to deny anxiety and stress. The best approach would be to give the patient opportunity to air the pent up feelings.

The Masochistic Personality

This personality seems to thrive on suffering and illness and disappointment. Some may look for their own unfavorable situation and they place themselves in a situation in which they get hurt. Frequently pain and punishment in these persons is confused. Punishment seems necessary as a means to relieve guilty feelings and pain may be the cross, the punishment to relieve the guilt. Success may mean revival of guilt feelings of childhood about early desires of being better than father, brother or sister. These patients will be overwhelmed again and again by their guilt feelings and their need to suffer. They may come into the hospital with chronic complaints like backaches, headaches and no particular medication will relieve the pain. They have to feel like martyrs. As a matter of fact, when the doctor tries to console them or to treat them with the most effective medication, there will still be pain left. The pain may even get worse with reassurance. What seems to be needed is recognition of his suffering attitude for his unconscious guilty feelings and to say, "I understand you have a heavy cross to bear," seems more acceptable to this patient than to say, "Your pain will go away shortly with this medication." For, to this person suffering is a way of life and a way of communicating.

The Schizoid Personality

This patient appears to be shy, rather seclusive and overly sensitive. He seems to be reserved and not much involved with other people. This may go as far as his becoming eccentric. This patient may prefer to be independent and alone. Yet, this patient is quite sensitive underneath. His seemingly uninterested, shy attitude is a defense against his over sensitivity. This person does not seem to be interested in much personal contact, but would like to be respected and left alone and, as such, appears more and more distant. Frequently, they are unable to express ordinary angry feelings and they withdraw from conflicts. This withdrawal and shyness has to be accepted and few demands for interpersonal relationship have to be expected from him. Yet, it seems best to be interested in this patient in a rather professional business like way.

The Cyclothymic Personality

This patient may show alternating depression and elation. When the patient is elated he may be active, alert, overly optimistic and enthusiastic. A serious operation may mean nothing and undergoing it will be too easily decided. They may underestimate their time for rehabilitation and may want to go home too early for proper healing. Weeks later the patient may come back worried, sleeping late, with loss of appetite, pessimistic and with little confidence. He may complain about his illness more than is warranted and he may feel that he would not be able to work. In the alternating pattern of behavior, it would be wise to hold middle ground, not to be swayed too much with the person's emotions, to be cautious when the patient is elated and to be more encouraging when he is depressed.

The Paranoid Personality

This patient is usually unwarrantedly suspicious and may have a tendency to blame others and to be distrustful of their methods. They may, at times, feel persecuted and slighted. They are hypersensitive and frequently feel self-righteous and show excessive self-importance. They also show great sensitivity toward criticism. This guarded, mistrustful patient may blame others for his illness. It is usually wise to explain exactly what will be done for treatment and to explain exactly what the illness is all about. Frequently, this patient may expect greater results because of their excessive feeling of self importance. They are ready to express their grievances of disappointment with their treatment at any time. Recognition of the feelings of his way of seeing the world seems helpful. An attempt to regain cooperation by realistic explanations and avoiding arguments and,

thus, more anxiety, seems the most feasible approach in this case.

The Explosive Personality

This patient, at times, may show gross outbursts of rage which are very unlike the usual personality. As a matter of fact, later on this patient may be apologetic about his behavior. Generally then, these patients are over responsive to environmental pressures. They seem not able to control their outbursts. It seems best to consider these explosive outbursts as exceptional behavior and to concentrate on their usual behavior and to accept the patient's apologies for his verbal aggressiveness and to go on with the treatment of the patient. This personality has been included so that we are aware of its existence.

The Passive Dependent Personality

This patient needs special attention and may give himself totally over to the physician, saying that he has total trust in his doctor. In the meantime, he may demand prompt repayment for his total trust. He may demand that the doctor accept him to make him feel wanted, to make him feel secure. Demanding care for physical comfort is specifically important in relieving the anxiety of these patients. Doctors and nurses may have to become aware not to be impatient or punitive in these cases. Certain limits seem necessary, but some extra care in diet or visiting privileges may relieve the anxiety expressed. The variant of this behavior is the passive aggressive personality. The aggressiveness here may be expressed in a passive way by procrastination or stubbornness. We find this behavior an expression of failure to find gratification in a good doctor-patient relationship.

Summary

I have briefly described above some of the personality types we may encounter in medical practice and have tried to explain some of the ways we may deal with the different personality constellations in the doctor-patient relationship. As such, I have elaborated on the sick role, the obligations and the privileges of the sick role and have described the dealings with the obsessive compulsive, the histrionic, the masochistic, the schizoid, the cyclothymic, the paranoid, the explosive and the passive aggressive personality and the dealings with them in the doctor-patient relationships.

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3. The operative report should be signed by the Attending/Surgeon.
4. The discharge summary should also be signed by the Attending in all cases.

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Cholecystitis, Pancreatitis and Pericarditis

LAURIER E. NOLIN, M.D. and JOHN F. REYNOLDS, M.D.

INTRODUCTION

The association of cholecystitis, pancreatitis and EKG abnormalities has been well documented in the literature. However, the association of pancreatitis has been found only rarely. In 1934, Drummond[1] reported an instance of cardiac irregularities occurring simultaneously with an acute pancreatitis. Dittler[3] reported a case of acute pancreatitis simulating a coronary thrombosis during which atrial fibrillation with rapid ventricular response was demonstrated by EKG. More recently, a group of French researchers demonstrated that EKG abnormalities associated with acute pancreatitis could be reverted to normal by the administration of an antiproteolytic substance called "zymofrene."

CASE PRESENTATION

A 19-year-old female presented herself at the Thayer Hospital on April 16, 1969, with complaint of excruciating right upper quadrant pain of 36 hours duration with associated nausea and vomiting. On examination, she appeared acutely ill. The temperature was 96 orally, pulse regular at 64 and blood pressure 110/80. Her chest was clear to auscultation and the heart sounds were normal without murmurs. Exquisite abdominal tenderness was present especially over the right upper quadrant with guarding. Laboratory data revealed a white count of 13, 250 with a shift to the left, heavy ketonuria and slight changes in her electrolytes with a sodium of 120 meq, potassium 4.3 meq, chloride 103 meq and CO_2 24. A biological profile showed elevation in bilirubin to 1.1 units, SGOT 80 units and alkaline phosphatase 23 units. A diagnosis of acute cholecystitis was made and she was taken to the operating room where under general anesthesia a tense and edematous gallbladder was removed. The surgeon, noted at the time that the pancreas was also edematous and showed evidence of moderate fat necrosis. The pathological report on the gallbladder was that of acute and chronic cholecystitis with cholelithiasis.

The postoperative course was unremarkable except for frequent complaints of low back pain. On the sixth postoperative day, the T tube was clamped, but due to nausea and vomiting this was unclamped 8 hours later. On the 8th postoperative day while ambulating, she complained of palpitations. Examination at the time was unremarkable her vital signs were normal. An EKG later showed a sinus tachycardia of 104, but was otherwise normal. She continued to complain of occasional fluttering in her chest over the following day and early that evening she was found in bed convulsing, cyanotic, and without an apical pulse. Emergency resuscitative measures were immediately instituted by the ward nurse, but on arrival at the scene her pulse was strong and regular and her blood pressure normal. Her respirations, however, were labored and she was still cyanotic. An EKG taken at the time showed a sinus tachycardia, a change in the electrical axis from 60° to 105°, large, broad and high P waves, iso-electric T waves over the limb leads and markedly decreased T wave voltage over the precordial leads with associated ST segment depression. She was transferred to the Intensive Care Unit and remained stable until 5:30 the following morning when she developed numerous premature ventricular contractions and short runs of ventricular tachycardia and ventricular flutter with associated convulsive attacks. Over the following 8 hours, she demonstrated a constant pattern of cardiac irregularities varying from premature atrial contractions to ventricular fibrillation, but generally having numerous multifocal premature ventricular contractions and short runs of ventricular tachycardia. During this period of time, she received approximately 3 grams of Pronestyl®, 2 grams of Lidocaine®, 4 mg. of Propranolol, 2 ampules of calcium gluconate and 100 meq of potassium chloride. A serum potassium obtained that morning was 3.6 meq. and her calcium normal. Later in the afternoon, her rhythm stabilized to a ventricular tachycardia at a rate of 110. She appeared to tolerate this rhythm well, as indicated by a blood pressure of 100 mm Hg systolic, an adequate urine output and normal cerebration. It was believed that maintenance doses of cardiac depressors could be used without resorting to overriding of the arrhythmia with a cardiac pacemaker. She maintained this rhythm for one hour and a half and subsequently reverted to a normal sinus rhythm. At that time, the heart sounds were muffled and a mid systolic squeak was heard very clearly for the first time. This rub was heard along the left sternal border over the 4th intercostal space. An EKG taken at that time showed a sinus rhythm at a rate of 100, a P-R interval of .16 seconds and a QRS duration of .08 seconds. The QT interval was .28 seconds. Large P waves were again noted and low T wave voltage and minor S T segment depression persisted. The following day her precordial friction rub became biphasic and was heard intermittently by numerous observers. Her cardiac irregularities subsided entirely over the following day. Subsequent EKGs showed inverted to biphasic T waves over the inferior and anterior leads and a decrease in P wave amplitude. Laboratory data consisted of chest x-rays, ASO titres, heterophile, L. E. cells, blood cultures, skin tests for T. B. and fungi, repeat electrolytes, serum electrophoresis and serum amylase – all were normal. She continued to improve and after four days in the Intensive Care Unit without premature contractions, she was transferred to a ward to be monitored by telemetry. Post op cholangiography was normal. She was discharged on her 27th post op day in good condition. Her discharge medication consisted of 500 mg. Pronestyl q.i.d. She has since been followed in the office and has remained free of cardiac symptoms or signs.

DISCUSSION

The relationship of gallbladder disease and heart disease is well appreciated in clinical medicine. Three categories are (1.) the association of heart and gallbladder disease with associated arrhythmias which improve after cholecystectomy; (2.) associated heart and gallbladder disease with angina type pain which improves after cholecystectomy; and (3.) electrographic abnormalities in the absence of heart disease with reversion to normal after cholecystectomy. The mechanism by which stimuli from a diseased gallbladder produce angina like pain and various arrhythmias is through vagal reflexes.[8–12] The nerve supply to the gallbladder is derived from the right vagus and splanchnic nerve through the celiac plexus. The sympathetic fibers for the gallbladder arise in the lateral horns of the four upper thoracic segments of the cord, whereas, the sympathetic fibers to the heart arise from the sixth thoracic through the first lumbar segment in the cord. The great splanchnic nerve, however, has branches which may be traced to the first and second sympathetic ganglia which communicate with the sensory pathways to the heart.

A similar reflex mechanism has been postulated in

patients with acute pancreatitis demonstrating associated EKG abnormalities.

In 1934, Drummond[4] described a case not unlike our present case. His description is as follows:

"She was obviously in extremis, and was given immediately ½ grain of morphea, and then as an afterthought 20 minims of adrenalin hypodermically. We lifted her on to the bed, and I found her pulse regular but fast and feeble. Almost immediately she went into another congestive spasm such as one is accustomed to associate with heart block, and with it her pulse became very slow and very irregular, with obvious intermissions and extrasystoles. The slowness and irregularity were associated with a pronounced feebleness of impulse, and this became progressively worse until all impulses at the wrist disappeared.

"She fell back on the pillows: her respirations, which had been getting shallower and more labored, ceased altogether, her pupils became widely dilated and cornea insensitive, and I pronounced her dead after failing to elicit any cardiac sounds with the stethoscope. Some half a minute later, before turning away, I felt her pulse, as one does mechanically under such circumstances, and to my surprise there was an isolated pulsation. After an appreciable pause came another and then another, and these became more frequent, stronger and more regular, until within a few minutes a strong, bounding pulse of 112 per minute was present. With the return of the pulse, the patient became more and more conscious, and an hour later was able to be moved into a near-by nursing home with a diagnosis of acute pancreatitis.

"This was confirmed at subsequent operation, and after drainage of the gallbladder she made an uneventful recovery."

EKG abnormalities have been noted for a long time in patients with acute pancreatitis. In addition to the vagal influence on cardiac functions hypocalcemia, hypokalemia, shock secondary to hypovolemia and the effect of circulating proteolytic enzymes have been incriminated. Hypocalcemia causes a prolongation of the Q-T interval; hypokalemia causes S T segment depression, flattening of the T waves and a large U wave. Shock will not generally cause EKG abnormalities in the absence of heart disease. The action of trypsin has been studied in experimental animals by the injection of Sodium Tauracholate into the pancreas with subsequent ligation of the pancreatic duct. The pancreas generally becomes hemorrhagic immediately and EKG's taken at 12 and 24-hour intervals show distinct changes. These changes are not consistent, but nevertheless indicate myocardial damage, but no cardiac abnormalities can be detected at autopsy. EKG changes described in the clinical state are similar to those manifested by our patient, namely, an increase in P wave amplitude over the inferior leads, the occasional presence of a significant Q wave in the same leads, depression of the ST segment to 0.1 mv. and diffuse flattening with occasional inversion of the T waves. In a study of 50 cases of acute pancreatitis, Lamburt[9] illustrated EKG abnormalities in fourteen cases and the presence of an infarction pattern in one case. Dittler[3] described a case in which the EKG indicated a myocardial infarction, but autopsy findings showed an acute pancreatitis and normal coronary arteries with no evidence of myocardial infarction. Gottesman[7] described five cases of acute pancreatitis in which the EKG was suggestive of myocardial infarction, but autopsy findings on one case showed patent coronaries and no evidence of infarction. In 1951, Vogel[15] published autopsy findings on a 44-year-old hypertensive woman who died of an acute hemorrhagic pancreatitis. His description of the heart is as follows:

"The myocardium contained scattered minute greyish-red streaks; these on histological section were formed of focal groups of muscle cells in which there were a striking loss of sarcoplasm and an absence of pyknosis of nuclei. In contrast, the reticulum and collagenous interstitial tissues remained intact and appeared as delicate honeycomb structures that were slightly infiltrated by lymphocytes and small mononuclear phagocytes."

Trypsin has been shown to have a thrombus producing effect when administered intravenously. There is, however, no experimental or pathological evidence to suggest that EKG changes in this condition may result from coronary artery occlusion since the administration of trypsin in anticoagulated and conrtol animals produces similar EKG changes. Recent work by Levy with "zymofrene" may support the direct effect of trypsin on the intracelluler metabolism.

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Dr. Nolin, 14 Gilman St., Waterville, Maine 04901.
Dr. Reynolds, 216 Main St., Waterville, Maine 04901.

X-Ray Of The Month*

This 53-year-old female initially had x-rays of the ankle because of an injury. Marked nodular thickening of the Achilles tendon with punctate calcification was noted.

Hypercholesteremic Xanthomata of the Tendons

Hypercholesteremic xanthomata of the tendons is one manifestation of hypercholesteremic xanthomastosis, a familial metabolic disturbance. The xanthomatous tumors are usually found on the extensor surfaces of the hands and feet and in the Achilles tendon. They are firm and non-tender; destructive bone lesions may be caused by pressure.

The condition is a familial one, although all members of the family may not be affected. It may also manifest itself with hypercholesterolemia, and xanthelasma of the skin, eyelids, blood vessels and endocardium. A recent paper reported a brother and sister with this condition, one of whom also had xanthomatous deposits in the cerebellum.

*From the Department of Radiology, Maine Medical Center, Portland, Maine 04102.

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Painful night leg cramps...

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One thing patients can sleep without, particularly patients with chronic disease conditions such as arthritis, diabetes or PVD, is painful night leg cramps. Although seldom the presenting complaint, night leg cramps can tie your patients up in painful knots. Now, just one tablet of QUINAMM at bedtime can usually bring an end to shattered sleep and needless suffering. Your patients will sleep restfully—gratefully—with QUINAMM, specific therapy to prevent painful night leg cramps.

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Brunswick, Maine

Dr. Rhoads Named President of the American Cancer Society

NEW YORK, N. Y. — Dr. Jonathan E. Rhoads, noted surgeon and director of the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania, was named President of the American Cancer Society at its Annual Meeting at the Waldorf-Astoria Hotel recently.

A native Philadelphian, Dr. Rhoads served for the past year as Vice President and President-Elect of the Society and was formerly chairman of its Medical and Scientific Committee. Dr. Rhoads is also John Rhea Barton Professor of Surgery at Penn.

Dr. Rhoads was graduated in 1928 from Haverford College where he was Phi Beta Kappa. He received his M.D. at Johns Hopkins in 1932. After earning a D.Sc. from Penn in 1940, he held a number of associate posts in the School of Medicine there and was a J. William White Professor of Surgical Research, 1949-51, becoming provost of the school in 1956.

A prolific writer and editor, Dr. Rhoads was most recently co-editor of "Surgery: Principles and Practice." He has written papers on surgical procedures in the management of liver, gallbladder, and pancreas ailments as well as having co-authored a paper on practical considerations in cancer surgery.

The noted surgeon was honored by the American Cancer Society in Philadelphia with its Humanitarian Award in 1963 for his outstanding contributions in the field of cancer control. Among his numerous affiliations, Dr. Rhoads is Chairman of the Board of Regents of the American College of Surgeons; a member of the American Academy of Arts and Sciences; the American Surgical Association; the Pan-Pacific Surgical Association; and a Regent of the American Philosophical Society. He is on the editorial board of the journal "Annals of Surgery."

Dr. Rhoads, who lives in Philadelphia, is married and the father of six children. His wife, Teresa Folin Rhoads, is also a physician and so are two of his sons, George and Jonathan, Jr.

The ACS also announced the election of Dr. H. Marvin Pollard, Professor of Internal Medicine at the University of Michigan School of Medicine at Ann Arbor, to the post of Vice President and President-Elect.

Currently chairman of the Medical and Scientific Committee of the Society, Dr. Pollard was Secretary-General of the World Congress of Gastroenterologists in 1958, and past president of the American Gastroenterology Association, and the American College of Physicians.

Born in Lamar, Colorado, Dr. Pollard received his M.D. degree from the University of Michigan in 1931. Following his internship, he served there also as instructor and assistant professor of internal medicine and was later chief of the school's Gastroenterology Section. He was formerly Consultant in Gastroenterology for the Veteran's Administration Hospital in Ann Arbor.

Dr. Pollard is a Director-at-large of the Society and was a board member of its Michigan Division.

American Cancer Society News Service Release.

Doctor, after all we've been through together...

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bacillary dysentery
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endocarditis
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gonorrhea
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Precautions: Nonsusceptible organisms may overgrow; treat superinfection appropriately. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).
Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage. Upon adverse reaction, stop medication and treat appropriately.

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News, Notes and Announcements

Department of Health and Welfare Division of Child Health Clinic Schedule (By Appointment Only)

Orthopedic Clinics

Augusta – Augusta General Hospital
1:00 p.m.: Apr. 16, Aug. 20, Dec. 17

Bangor – St. Joseph Hospital
9:00 a.m. and 1:00 p.m.: Jan. 22, Mar. 26, May 28, July 23, Sept. 24, Nov. 19
Half-day sessions, 1:00 p.m.: Feb. 26, Apr. 23, June 25, Aug. 27, Oct. 22, Dec. 24

Ellsworth – Maine Coast Memorial Hospital
9:00 a.m.: Mar. 19, June 18, Sept. 17, Dec. 17

Fort Fairfield – Community General Hospital
9:00 a.m.: Jan. 12, Mar. 9, May 11, July 13, Sept. 14, Nov. 9

Fort Kent – Peoples Benevolent Hospital
9:00 a.m.: Jan. 13, Mar. 10, May 12, July 14, Sept. 15, Nov. 10

Houlton – Aroostook General Hospital
9:00 a.m.: Jan. 15, Mar. 12, May 14, July 16, Sept. 17, Nov. 12

Lewiston – Central Maine General Hospital
9:00 a.m. and Bracing Clinic 12:30 p.m.: Jan. 16, Feb. 20, Mar. 20, Apr. 17, May 15, June 19, July 17, Aug. 21, Sept. 18, Oct. 16, Nov. 20, Dec. 18

Machias – Down East Community Hospital
9:00 a.m.: Feb. 20, May 22, Aug. 28, Nov. 20

Portland – Maine Medical Center
10:30 a.m.: Jan. 5, 12, 19, 26, Feb. 2, 9, 23, Mar. 2, 9, 16, 23, 30, Apr. 6, 13, 27, May 4, 11, 18, June 8, 15, 22, 29, July 6, 13, 20, 27, Aug. 3, 10, 17, 24, 31, Sept. 14, 21, 28, Oct. 5, 12, 19, Nov. 2, 9, 16, 23, 30, Dec. 7, 14, 21, 28

Presque Isle – Arthur R. Gould Memorial Hospital
9:00 a.m.: Jan. 14, Mar. 11, May 13, July 15, Sept. 16, Nov. 11

Waterville – Thayer Hospital
Time staggered by hospital: Jan. 28, Feb. 25, Mar. 25, Apr. 22, May 27, June 24, July 22, Aug. 26, Sept. 23, Oct. 28, Nov. 25, Dec. 23

Cardiac Clinics

Bangor – St. Joseph Hospital
9:00 a.m.: Jan. 9, 23, Feb. 13, 27, Mar. 13, 27, Apr. 10, 24, May 8, 22, June 12, 26, July 10, 24, Aug. 14, 28, Sept. 11, 25, Oct. 9, 23, Nov. 13, 20, Dec. 11, 18

Portland – Maine Medical Center
9:00 a.m.: Jan. 2, 9, 16, 23, 30, Feb. 6, 13, 20, 27, Mar. 6, 13, 20, 27, April 3, 10, 17, 24, May 1, 8, 15, 22, 29, June 5, 12, 19, 26, July 3, 10, 17, 24, 31, Aug. 7, 14, 21, 28, Sept. 4, 11, 18, 25, Oct. 2, 9, 16, 23, 30, Nov. 6, 13, 20, 27, Dec. 4, 11, 18

Pediatric Clinics

Bangor – St. Joseph Hospital
1:30 p.m.: Jan. 23, Feb. 27, Mar. 27, Apr. 24, May 22, June 26, July 24, Aug. 28, Sept. 25, Oct. 23, Nov. 20, Dec. 18

Fort Kent – Peoples Benevolent Hospital
10:00 a.m.: Mar. 25, July 22, Nov. 25

Houlton – Madigan Memorial Hospital
1:30 p.m.: Apr. 8, Aug. 12, Dec. 9

Presque Isle – Arthur R. Gould Memorial Hospital
1:30 p.m.: Jan. 28, Feb. 25, May 27, June 24, Sept. 23, Oct. 28

Waterville – Thayer Hospital
Time staggered by hospital: Jan. 14, Feb. 11, Mar. 11, Apr. 8, May 13, June 10, July 8, Aug. 12, Sept. 9, Oct. 14, Nov. 11, Dec. 9

Cleft Palate

Portland – Maine Medical Center
10:00 a.m.: Feb. 10, May 12, Sept. 8, Nov. 10

Mentally Retarded Preschool

Waterville – Thayer Hospital
9:00 a.m.: Jan. 7, 21, Feb. 4, 18, Mar. 4, 18, Apr. 1, 15, 29, May 6, 20, June 3, 17, July 1, 15, 29, Aug. 5, 19, Sept. 2, 16, 30, Oct. 7, 21, Nov. 4, 18, Dec. 2, 16, 30
Lewiston – Central Maine General Hospital
9:00 a.m.: Jan. 12, Feb. 9, Mar. 9, Apr. 13, May 11, June 8, July 13, Aug. 10, Sept. 14, Oct. 12, Nov. 9, Dec. 14
Lewiston – St. Mary's Hospital
9:00 a.m.: Jan. 26, Feb. 23, Mar. 23, Apr. 27, May 26, June 22, July 27, Aug. 24, Sept. 28, Oct. 27, Nov. 23, Dec. 28

Cystic Fibrosis

Portland – Maine Medical Center
9:00 a.m.: Jan. 20, Feb. 17, Mar. 17, Apr. 21, May 19, June 16, July 21, Aug. 18, Sept. 15, Oct. 20, Nov. 17, Dec. 15
Lewiston – Central Maine General Hospital
9:00 a.m.: Jan. 2, Feb. 6, Mar. 6, Apr. 3, May 1, June 5, July 3, Aug. 7, Sept. 4, Oct. 2, Nov. 6, Dec. 4

Family Planning

Augusta – Augusta General Hospital
9:00 a.m.: Jan. 13, Feb. 10, Mar. 10, Apr. 14, May 12, June 9, July 14, Aug. 11, Sept. 8, Oct. 13, Nov. 10, Dec. 8
Bangor – Eastern Maine Medical Center
a.m. clinic: Jan. 2, 16, Feb. 6, 20, Mar. 6, 20, Apr. 3, 17, May 1, 15, June 5, 19, July 3, 17, Aug. 7, 21, Sept. 4, 18, Oct. 2, 16, Nov. 6, 20, Dec. 4, 18
Portland – Maine Medical Center
Clinics are held bi-weekly, by appointment only

Maine Physician on AMA's New Committee on Private Practice

AMA's New Committee on Private Practice, created by the House of Delegates at the Denver Clinical Convention, recently held its organizational meeting. Members are W. B. Hildebrand, M.D., Menasha, Wis., chairman; Robert E. Tschantz, M.D., Canton, Ohio, vice-chairman; C. Willard Camalier, Jr., M.D., Washington, D.C.; Burns A. Dobbins, M.D., Fort Lauderdale, Fla.; Frank H. Green, M.D., Rushville, Ind.; Warren A. Lapp, M.D., Brooklyn, N.Y.; Clinton S. McGill, M.D., Portland, Ore.; John G. Morrison, M.D., San Leandro, Calif.; Tom E. Nesbitt, M.D., Nashville; Andrew L. Thomas, M.D., Chicago; *George W. Wood, III, M.D.*, Brewer, Me. The committee is a component of the Council on Medical Service.

Postgraduate Course in Laryngology and Bronchoesophagology

The Department of Otolaryngology of the Eye and Ear Infirmary of the University of Illinois Hospital and the College of Medicine of the University of Illinois at the Medical Center, will conduct a postgraduate course in Laryngology and Bronchoesophagology from April 6 through 17, 1970. This course is limited to fifteen physicians and will be under the direction of Paul H. Holinger, M.D. It will be held largely at the Eye and Ear Infirmary, 1855 West Taylor Street, Chicago, and will include visits to a number of other Chicago hospitals. Instruction will be provided by means of animal demonstrations and practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics, as well as didactic lectures.

Interested registrants will please write directly to the Department of Otolaryngology, College of Medicine, University of Illinois at the Medical Center, P.O. Box 6998, Chicago, Illinois 60680.

Seminar on Cancer of the Breast

The 9th annual Seminar on Cancer of the Breast will be held in Denver, Colorado, May 14, 15 and 16, 1970 at the Brown Palace Hotel.

For additional information on this Seminar, you may write to: Wendell P. Stampfli, M.D., Chairman of Local Arrangements, Department of Radiology, St. Luke's Hospital, Denver, Colorado.

Letter to the Editor

To the Editor:

The Maine Medical Association's Priority Committee has appointed a Paramedical Personnel Subcommittee to explore needs in this area, and to propose solutions. A meeting was held in Waterville on January 7, 1970, at which time there was complete agreement on obtaining a data base as the starting point. All members of the M.M.A. will soon receive a questionnaire regarding the development and possible use of paramedical personnel.

We hope that all members will take the two minutes to check the list, and to add comments.

GEORGE W. HALLETT, M.D.
Chairman, Paramedical Personnel Subcommittee
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Hasn't the skipper had enough excitement for one day?

For the patient who has been through an accident, the worry and anxiety following the mishap may actually heighten the perception of pain. This is why there's a classic ¼ grain *sedative* dose of phenobarbital in Phenaphen with Codeine—to take the nervous "edge" off, so the rest of the formula can control the pain more effectively.

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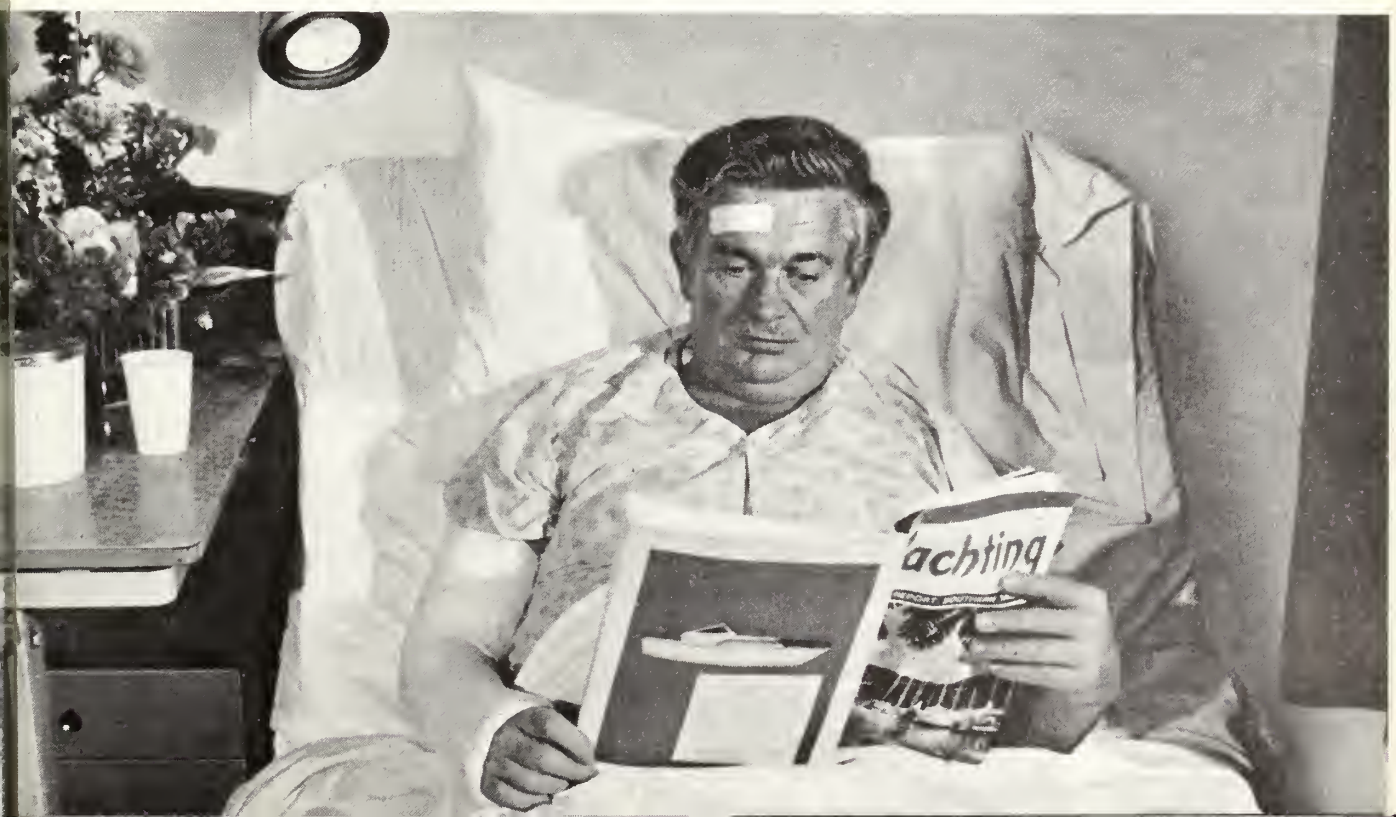

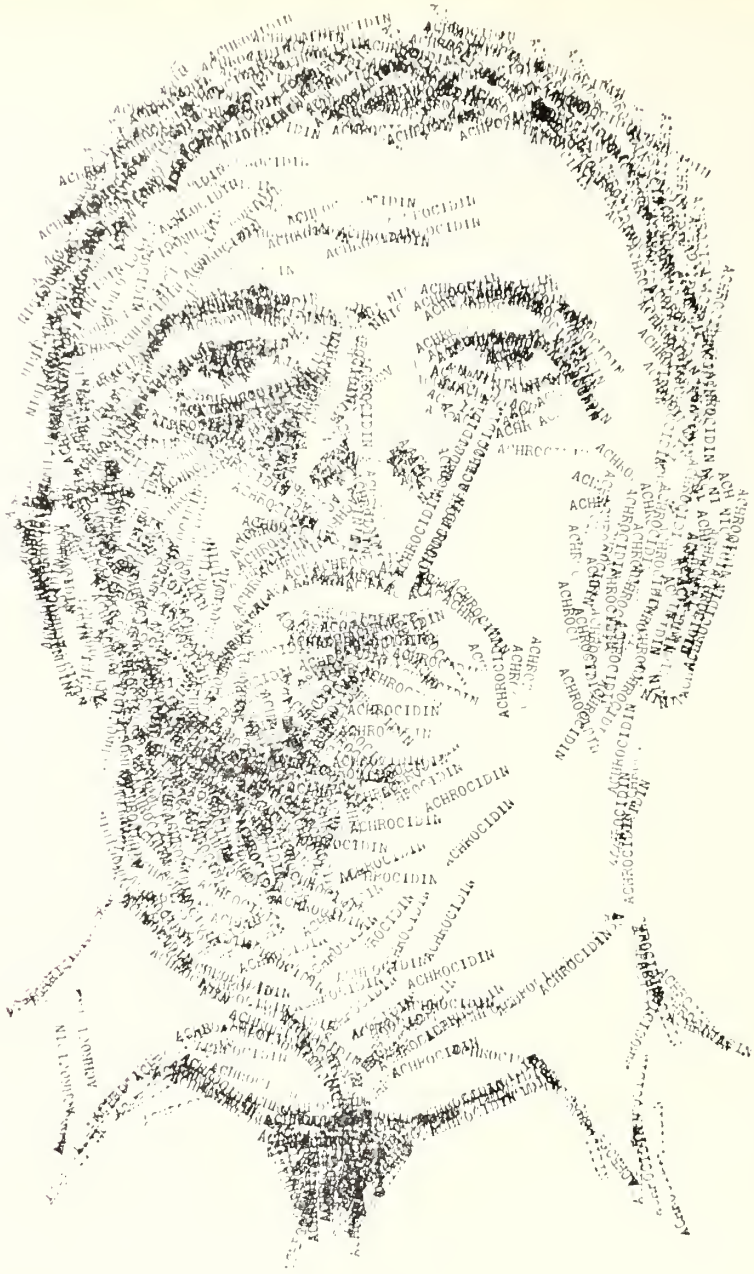

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Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.
Precautions: Drowsiness, anorexia, slight gastric distress can occur. In excessive drowsiness, consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).
Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliat dermatitis; photosensitivity; onycholysis, discoloration. *Kidney*—dose-related rise BUN. *Hypersensitivity reactions*—urtica angioneurotic edema, anaphylaxis. *Intracra* —bulging fontanels in young infants. *Tee* yellow-brown staining; enamel hypopla *Blood*—anemia, thrombocytopenic purp neutropenia, eosinophilia. *Liver*—cholestasis high dosage.
Upon adverse reaction, stop medication treat appropriately.

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Contraindications: Sensitivity to either component. ***Precautions:*** Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped. ***Adverse Reactions:*** Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, *Paraflex* (chlorzoxazone) may possibly have been associated with gastrointestinal bleeding. While *Paraflex* (chlorzoxazone) and chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately eighteen patients, it was not possible to state that the dysfunction was or was not drug induced. ***Usual Adult Dosage:*** Two tablets q.i.d. ***Supplied:*** Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.:* Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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Contraindications: Edema, danger of cardiac decompensation; history or symptoms of peptic ulcer, renal, hepatic or cardiac damage; history of drug allergy, history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently. Large doses of the alka formulation are contraindicated in glaucoma.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Persistent or severe dyspepsia may indicate peptic ulcer; perform upper gastrointestinal x-ray diagnostic tests if drug is continued. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with caution in the first trimester of pregnancy and in patients with thyroid disease.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. Patients should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention), skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make complete blood counts at weekly intervals during early therapy and at 2-week intervals thereafter. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The more common are nausea and edema. Swelling of the ankles or face may minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the dru should be discontinued with the a pearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediatel before or after meals or with milk minimize gastric upset. Drug rash occasionally occurs. If it does, promptly discontinue the drug. Agranulocytosis, exfoliative derma

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Stevens-Johnson syndrome, s syndrome (toxic necrotizing ermolysis), or a generalized gic reaction similar to serum ess may occur and require anent withdrawal of medica- Agranulocytosis can occur enly in spite of regular, repeated al white counts. Stomatitis rarely, salivary gland enlarge- may require cessation of treat- Such patients should not ve subsequent courses of the Vomiting, vertigo and languor occur. Leukemia and leukemoid ions have been reported. While efinitely attributable to the a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, hypersensitivity angiitis, pericarditis and several cases of anuria, glomerulonephritis and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Rheumatoid Arthritis: Initial: 3 to 6 capsules daily in 3 or 4 equal doses. Trial period: 1 week. Maintenance dosage should not exceed 4 capsules daily; response is often achieved with 1 or 2 capsules daily. In selecting the appropriate dosage in any specific case, consideration should be given to the patient's weight, general health, age and any other factors influencing drug response. (B)46-070-C

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Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy may be avoided by remaining within the recommended limits of dosage. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving). Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension. Daily doses in excess of 300 mg. should be used only in severe neuropsychiatric conditions.

Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequently, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—Changes in the terminal portion of the electrocardiogram have been observed in some patients receiving the phenothiazine tranquilizers, including Mellaril (thioridazine). While there is no evidence at present that these changes are in any way precursors of any significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients previously showing electrocardiographic changes. The use of periodic electrocardiograms has been proposed but would appear to be of questionable value as a predictive device. *Other*—A single case described as parotid swelling.

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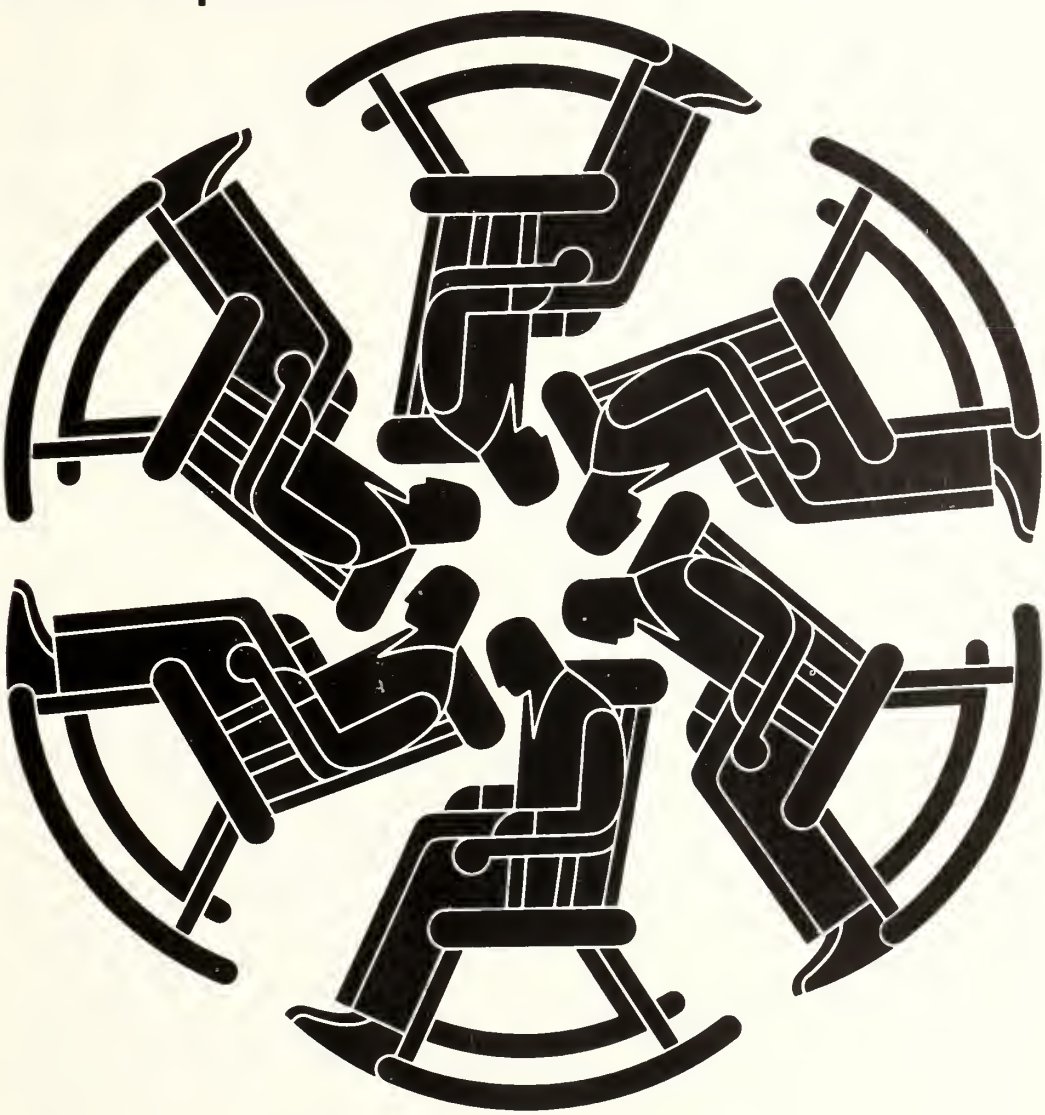

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Usual dosage is one tablet b.i.d.

Indications: Nutritional supplementation in conditions in which water-soluble vitamins are required prophylactically or therapeutically.

Warning: Not intended for treatment of pernicious anemia or other primary or secondary anemias. Neurologic involvement may develop or progress, despite temporary remission of anemia, in patients with pernicious anemia who receive more than 0.1 mg of folic acid per day and who are inadequately treated with vitamin B_{12}.

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Countersigned by:

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Article I [illegible]finiti[illegible]

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Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported, in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium and BUN during therapy, particularly in patients with suspected or confirmed renal or hepatic insufficiency (e.g., certain elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—their combined use can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk; thus adverse reactions which have occurred in adults may occur in the fetus or newborn infant. Rarely, thrombocytopenia or pancreatitis has developed in newborn infants whose mothers had received thiazides during pregnancy. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte determinations. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Adjust dose of antihypertensive agents given concomitantly.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, altered carbohydrate metabolism, hyperbilirubinemia, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules.

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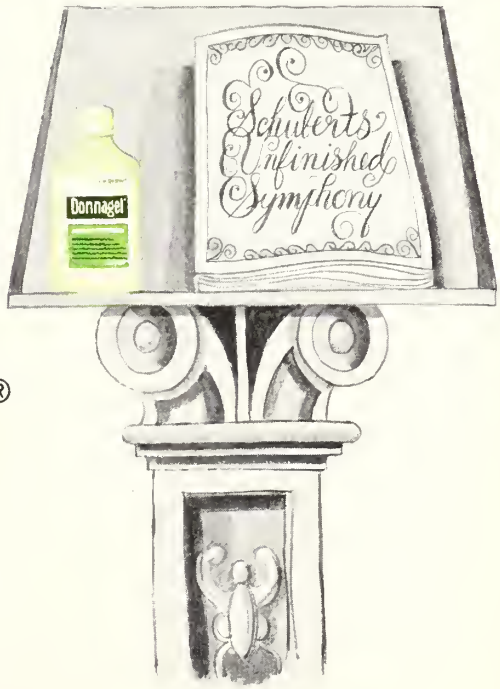

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uid ounce contains: Kaolin, 6 Gm.; Pectin, 142.8 mg.; Hyoscyamine sulfate, mg.; Atropine sulfate, 0.0194 mg.; Hyoscine hydrobromide, 0.0065 mg.; ı benzoate (preservative), 60 mg.; Alcohol, 3.8%.

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When disease is ruled out and psychic tension is implicated

Valium® (diazepam)

helps relax the patient and relieve his somatic symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms have occurred following abrupt discontinuance. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation, have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epilept an increase in convulsive episodes has been reported. Sympathomimetic card vascular effects reported include ones such as tachycardia, precordial pa arrhythmia, palpitation, and increased blood pressure. One published rep described T-wave changes in the ECG of a healthy young male after ingestion diethylpropion hydrochloride; this was an isolated experience, which has not be reported by others. Allergic phenomena reported include such conditions as ra urticaria, ecchymosis, and erythema. Gastrointestinal effects such as diarrhe constipation, nausea, vomiting, and abdominal discomfort have been reporte Specific reports on the hematopoietic system include two each of bone marr depression, agranulocytosis, and leukopenia. A variety of miscellaneous adver reactions have been reported by physicians. These include complaints such as d mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreas libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tab daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet thr times daily, one hour before meals. If desired, an additional tablet may be given midevening to overcome night hunger. Use in children under 12 years of age is r recommended.

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■ to help restore and stabilize the intestinal flora

■ for fever blisters and canker sores of herpetic origin

Lactinex contains both *Lactobacillus acidophilus* and *L. bulgaricus* in a standardized viable culture, with the naturally occurring metabolic products produced by these organisms.

Lactinex has been shown to be useful in the treatment of gastrointestinal disturbances, and for relieving the painful oral lesions of fever blisters and canker sores of herpetic origin.[1,2,3,4,5,6,7,8]

No untoward side effects have been reported to date.

Literature on indications and dosage available on request.

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References:

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* ESTHER M. KENNARD, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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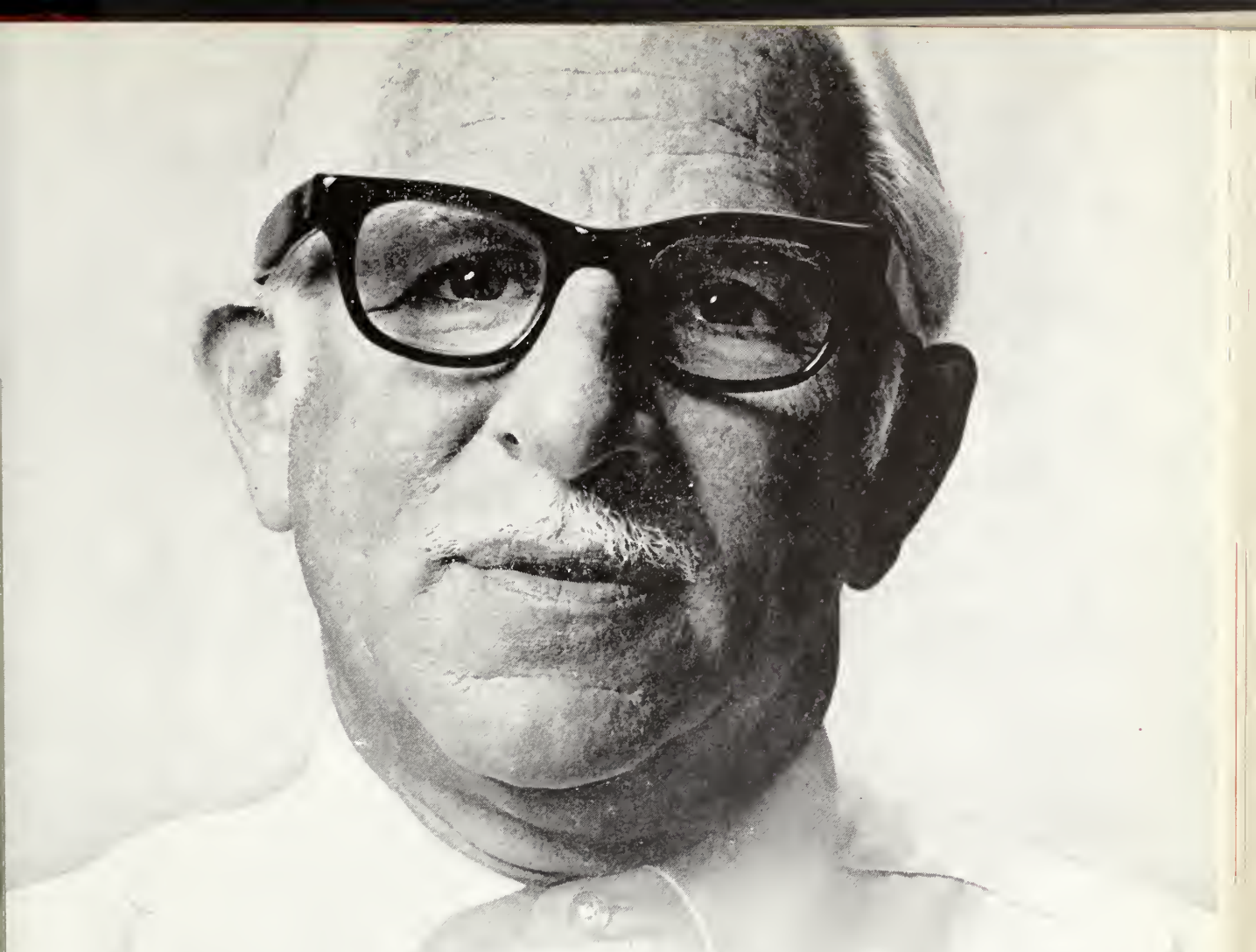

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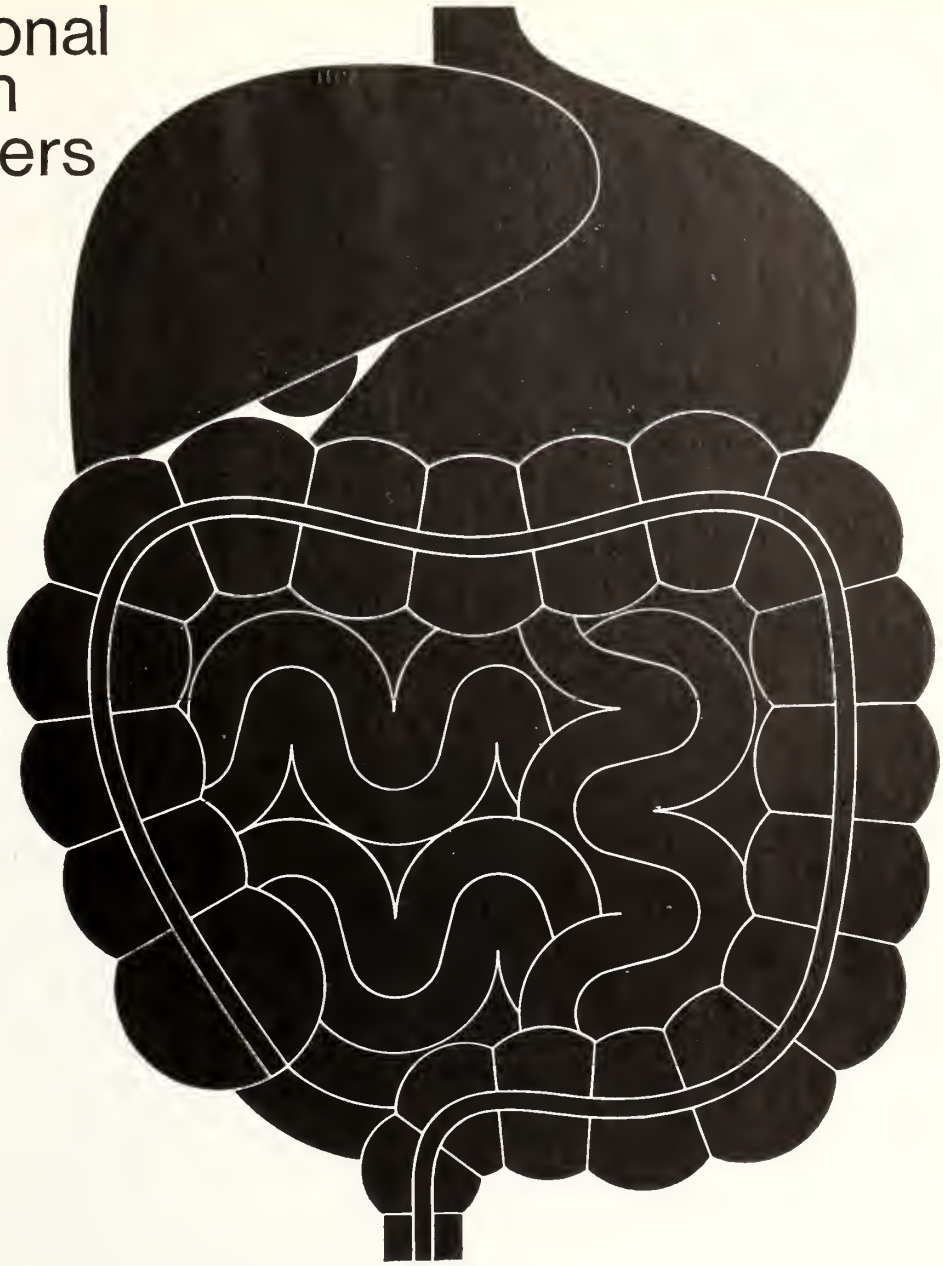

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Drugs, Sports and Doping*

KENNETH S. CLARKE, PH.D.**

In 1960, a cyclist died at the Rome Olympic Games after collapsing during a 67 mile road race on a hot day; he had taken a vasodilator drug. In 1967, two well-known cyclists, one French, one British, also died in a road race; the drug this time for both was an amphetamine.

Yet, one of the most difficult problems that can face anyone in athletics remains to respond effectively to an athlete who is curious about drugs. Unlike the escape-oriented user of drugs outside sports, the athlete's curiosity is task-oriented; to participate in sports, he has already accepted formidable risks. If a flat negative is given, therefore, the athlete is likely to shop elsewhere for this and other advice as well. If a superficial, cynical, or inaccurate response is given, the athlete is done a disservice. But if a frank discussion is utilized that puts the use, abuse, and effectiveness of drugs into a functional perspective, the athlete has the opportunity of developing attitudes that could help him respect the proper role of drugs in sports and in life.

The professional literature has not made it easy for the conscientious person who realizes his limitations in discussing drugs. A variety of definitions and solutions exists concerning what is good use of drugs, what is questionable use of drugs, and what is "doping." Being neither lawyer, pharmacologist, nor physician, I do not have the expertise to exhaust the detail of the good and bad of drugs. But as an educator, I would like to share some thoughts as to the essentials of a drug control perspective.

ESSENTIAL #1: PURPOSES OF DRUGS

The first essential concerns purpose. To use a drug, there must be justifiable purpose. The justification of a drug is the particular anticipated benefit it can offer in the treatment of a particular clinical condition.

Clinical purposes of drug administration can be categorized with their benefits as either "to cure," "to control," or "to comfort." The use of penicillin after a diagnosis of a strep infection is an illustration of the first purpose. The use of insulin to keep a diabetic athlete healthy is an illustration of the second. The use of aspirins and liniments illustrates the third purpose.

A fourth and more nebulous purpose is "to improve." The use of vitamins and tonics are illustrations. The use of LSD and marijuana are also illustrations. The use of amphetamines and anabolic steroids are further illustrations. To put this in perspective, a medical diagnosis of a significant deficiency must precede treatment if the "improve" purpose is to have clinical justification.

Purpose, therefore, must assume a competent decision as to the nature of the condition and a competent selection as to a particular drug that may provide the needed benefit.

ESSENTIAL #2: EFFECTS OF DRUGS

Talking about purposes of drugs is one thing; their subsequent effects are another. To be effective, a drug must markedly alter the body's processes. The nature and degree of this alteration is highly variable – from occasion to occasion as well as from person to person. Further, anything so potent to alter the body's metabolism can harm as well as benefit the consumer. One anesthesiologist has calculated that 32 factors can alter drug behavior in the body.[1] Dosage, purity, timing, solubility, and tolerance are examples of such factors. Consequently, the athlete should respect the fact that if he chooses to dabble with a drug, he may be accepting some serious hazards for some unreliable benefits.

Justification of a drug therefore also requires a sufficient awareness of its hazards to arrive at competent judgement that the potential benefits are worth the potential risks. When the patient is an athlete, the requirements for this judgement are compounded: The analysis of these effects must be task-oriented as well as clinically oriented. The clinical use of a drug for an athlete may render him ill-prepared to participate safely in competition. For example, before succinylsulfathiazole was selected for prophylactic use by the U.S. Olympic Team to minimize the threat of diarrhea in Mexico City, it was tested to see if such use would backfire by decreasing the performance capabilities of the user.[2] As already demonstrated, athletes on potent stimulants risk the hazards of exertion beyond a normal level of fatigue. Another example is the use of pain-killers to return an injured athlete to play. Here, specificity of justification is paramount. The customary criteria for "good medicine" still apply, i.e., an ethical relationship, an accurate diagnosis, and an informed knowledge of the consequences of drug intervention. The athletes must rely on physicians' respect for these criteria to keep their return to play with an injury courageous acts worthy of the traditions of athletics and not acts of folly that shortens their careers.

ESSENTIAL #3: CONTROLS

The third essential of a drug control perspective is the matter of controls to protect the consumer-athlete

*Presented at the West Virginia University Sports Medicine Seminar, Morgantown, September 20, 1969.

**Coordinator of Continuing Education, American Academy of Orthopaedic Surgeons, Chicago, Illinois.

from drug producers, practitioners, and himself. Three types of controls exist – laws, ethics, and education.

The law states that any new drug developed for human use must first undergo a long period of testing under tightly controlled conditions. A reasonable and beneficial purpose must be declared; effects are carefully noted. Animal testing precedes human testing if any question as to safety exists. Only physicians who are registered in one of the approved controlled studies can use the drug until released by the FDA as either an over-the-counter drug or prescription drug. If a prescription drug, it can be dispensed only after a physician prescribes it for *his* patients and for clinical purposes. The law and the ethics of the medical and pharmaceutical professions are quite specific on this point. Over-the-counter or prescription, a drug's advertisements can neither exceed its reasonably proven benefits nor disguise its reasonably proven hazards.

For example, in the 1940's, a supplier of athletic trainers' supplies and first aid preparations was reprimanded by the Federal Trade Commission (FTC) for excessive claims regarding germ-killing, prevention of certain diseases, liniment powers, the energy qualities of their sugar tablets, and similar pseudomedical treatments.

In 1961, the Food and Drug Administration (FDA) seized another company's food supplement as a drug being falsely promoted to coaches as an aid to physical endurance, prevention of fatigue, lessening muscle soreness, and improving physical efficiency. Seized at the same time was another product by this company labeled to improve resistance to bruising, bleeding, and the common cold. The FDA charged that the product would not be effective for the conditions represented in the labeling.

More recently, in 1966, the FDA acted to withdraw dimethylsulfoxide (DMSO) from its human trial status. The problems with this potent solvent was that popular publicity had jumped the gun on the evaluation of the drug in its preliminary testing stages. The resulting tremendous clamor for DMSO's purported sensational qualities (e.g., pain-killing) and the easy access to impure DMSO brought pressure on physicians who 1) did not have the benefit of investigative reports that would define the hazards as well as values associated with particular circumstances and patients; and 2) would not have been using the drug ethically or legally unless in a registered study for one of the several sponsoring drug companies. Yet, even though the drug was still restricted only to authorized clinical investigations conducted by registered medical personnel, even though the drug had particular hazards in the athletic setting,† this did not hinder some of the principals involved to extol the virtues of DMSO to coaches and trainers.[3]

A reasonable depth of search has provided only these three instances of direct governmental intervention in protecting the athlete from the drug producer. I could raise this figure to four if you would accept the action by another country against a U.S.-made product called Strawberry Ointment (for abrasions) because it contained no strawberries. Court-convicted cases of surreptitious drug abuse by or for the consumer-athlete in the U.S. were not researched, but only one such case has ever come to my attention.

Laws therefore are with us to protect the consumer-athlete from inadvertent as well as frank misuse of drugs. We also have had authoritative statements on drug abuses in sports – for those who wish to read them – from such as the AMA Committee on Medical Aspects of Sports; the American Association for Health, Physical Education, and Recreation; British Medical Association; the Federation for International Sports Medicine; the Pacific-8 Team Physicians, etc., etc. The interest and vigilance among responsible people against drug abuse have not been lacking.

But to turn to the law or the regulation for controls of drugs in sports is a hazard in itself. To turn to the law (as to turn to drugs) is often to rely on it. To rely on the law requires faith to the letter in a definition of right and wrong that punishes the undesirable while not inhibiting the desirable – with an enforcement arm to match. This is too much to ask for those who make and enforce laws.

Essential #4: A Concept of Doping

What is needed instead of more laws is a more manageable concept of the sports problem called "doping." This problem can be outlined as follows: 1) to strive to one's fullest to win is fundamental to competitive sports; 2) the popular press, capitalizing on the public's intrigue with "reasons" for successful and unsuccessful strivings, periodically return to an indiscriminate debate on "doping" (the use and influence of drugs in the quest of athletic advantage); 3) the athletic trainer and team physician are known to have a number of items at their respective disposal that would qualify as drugs; 4) indiscriminate debates on drugs lead to indiscriminate approaches to control and also confuse doping with many honorable practices in the field of sports medicine.

There is no question but that a black market availability of "doping" drugs exists, and a market does not exist where there are no consumers. As long as the athlete feels that his opponent has an advantage by taking a drug, he is tempted to dabble as well. This is why I regret that the International Olympic Committee felt it had to incorporate drug tests for the Mexico City Olympics, though there undoubtedly was some evidence of drug abuse among athletes – especially endurance cyclists from European countries – to try testing as a deterrent:

†Beyond the adverse effects attributed to DMSO when applied to the skin under *controlled* conditions, the athlete would risk absorbing toxic ingredients found in liniments, turf fertilizers, line markers, and what have you, as well as premature return to play by masking injury pain.

First, detection tests can be valid for only a portion of the drugs contested and of the athletes competing, and then can be reliable only within a certain time span. Many foreign substances in the urine at the time of testing can be picked up by gas chromatography. To be utilized, I understand you need about $10,000 for the apparatus and a team of 4-5 persons to handle the apparatus. Working around the clock, however, the yield in that time would be only about 20 specimens. The real hooker, however, is getting the specimen. Even if a more efficient testing apparatus appeared, there would have to be a very tenacious and incorruptible man for every athlete to get the specimen shortly after his performance; and if any athlete is to be suspected and tested, all should be suspected and tested. Further, athletes using drugs such as the anabolic steroids would still not be detected.

Second, and most important, in my eyes, *it has yet to be proved that the dabblers have the edge on the non-dabblers, that any drug indeed does reliably enhance performance beyond one's normal capabilities.* The athlete and his doting public are led to believe that dabblers are getting away with something because they read about the testing of winners. Have they considered that the place to look for the dabblers could be among the losers? Officials of a 1967 Italian Cyclist Road Race found three amphetamines users: they had come in 11th, 12th, and 14th. At the Winnepeg Pan-Am Games, Canadian officials sampled broadly and also found definite amphetamine use among the losers.

Therefore, I fear that the Mexico City tests for Olympic athletes served primarily to publicize an undeserved credibility of advantage from doping in the eyes and ears of our millions of young and impressionable sports participants. Deaths among cyclists from use of drugs has been a national scandal in France, and a French federal law is now on the books for curbing this abuse. Whether or not this aided the IOC decision I do not know, but such an outcome of doping is hardly what I would like pepetuated among our youthful athletes through controls that make doping appear enticing. Let's look at the amphetamines and anabolic steroids in this regard.

Amphetamines

The most common drug associated with doping in sports, is the amphetamine or "pep pill." One early study concerning its effects on performance suggested that under certain conditions, performance levels were improved; this was attributed to an over-riding of the body's fatigue-producing safeguards. Further studies, however, have not been very corroborative. One review and analysis has indicated the action of amphetamines is not a lessening of the fatigue effect but an improvement of sustained attention. This is a significant distinction. In order to improve performance reliably by amphetamines, three elements were found to be required:[4]

1. an existing sustained attention to the task
2. habituation to the task
3. habituation to the drug

Consequently, to arrive at any benefit with any reliability, the task must be sufficiently simple and uniform to permit sustained attention and habituation. Most sports tasks are complex and variable. Those athletes with tasks that might meet these criteria must not only guess correctly the timing and dosage to get the desired effect during performance; to arrive at the benefits with any reliability, they must also paradoxically risk deteriorated performance from being habituated to the drug. Habituation to amphetamines can lead to problems of insomnia, headache, acute anxiety states, and circulatory collapse. The state of being habituated to a drug is a bad enough problem.

Research on the amphetamines also suggest that a person's judgment can be impaired, in the sense that he overestimates significantly the beneficial effect of the drug on his performance.[5] This finding underlies the common impression among amphetamine users that the drug is helpful, an impression that interferes with educational programs against such use.

Anabolic-Androgenic Steroids[6]

While considerable attention has been given to amphetamines, interest in the use of another type of drug has been increasing in the athletic setting. The androgenic-anabolic steroids, so named because they resemble chemically and functionally the male sex hormones, are being taken by some athletes with the intent of gaining weight for sports where weight is considered an advantage. These drugs are categorically condemned for the athlete; their effects are far more subtle and insidious than those associated with pep pills.

The clinical purpose of the drugs is in the treatment of deficiencies – deficiencies not related to healthy athletes: some anemias, osteoporosis, and chronic debilitating illnesses as well as male hormone deficiencies. Small doses are claimed to bring about weight increases in underweight children and to accelerate growth in some children with growth retardation. However, even under clinically justified conditions and close medical management, these drugs are so potent and have demonstrated such undesirable side effects that their use is advised only after special consultation.

While the college-age athlete is the focus of debate on the dabbling with anabolic steroids, it must be understood that there would be differences in some of the drugs' effects and hazards between prepubertal, pubertal, and postpubertal males. This is a serious fact considering that the young athlete is noted for trying to emulate his older counterpart.

From grade school through junior high school or early high school level, athletes receiving the steroids definitely risk stunted growth (because of premature closing of long bone growth centers) and markedly supressed testosterone production by the developing testes.

For the adult or postpubertal athlete, the growth and development factors no longer apply. This population may consider sufficiently inhibiting the drugs' side-effect to which they are vulnerable – a decreased libido. The size and function of the testicles are known to revert to the prepubertal stage during extended administration of these steroids.

It should be further noted that the above warnings are based on evidence compiled for the most part from the use of drugs under medically supervised conditions and *where clinical deficiencies had been diagnosed giving purpose to the drugs.* Where the consumer is a healthy male without deficiencies, significant new problems – clinical and ethical – are posed. Increased chance for prostate cancer is among that being discussed. Many years will have to pass before any evidence of such harm can be demonstrated. The delay in appearance of these and other known and unknown effects can easily lead to mistaken etiologies, misdiagnoses and inappropriate treatment.

Finally, for those who are not impressed even by these effects, a controlled study in Southern California revealed no significant differences between subjects who received an anabolic steroid and those who received a placebo, with respect to strength, motor performance, work capacity, and other such measurements taken.[7] Also, some clinicians are attributing any increased weight in the normal male from steroid use to increased appetite or water retention or both.

All known and unknown risks consequently are apparently taken for nothing. There are less heroic and more honorable means of trying to add muscular weight to increase performance.

A Definition of Doping

The problem of doping can be approached best by reducing its issues to the essentials of a definition of appropriate conduct: *The issue of doping in sports, if limited to the use of a prescription drug for other than clinically-justified purposes, lends itself to manageable and defensible controls by law, ethics, and education.*

By limiting doping to prescription drugs, we do not have to confuse the less potent over-the-counter drugs with those allegedly giving unfair advantage. Since potency is required to cure or to control a significant clinical condition, it can be seen that any benefit of over-the-counter drugs would not be an unusual enhancement but would be limited to minor problems and then primarily related to the purpose "to comfort" in the sense of relief from nuisance aches and pains.

By limiting doping to prescription drugs, roles and responsibilities and prerogatives are defined clearly: Only a physician can provide such a drug to the athletes. By limiting drugs to clinically-justified purposes, the ethics of both sports and medicine are upheld.

As for abuses to doping as defined above, the hue and the cry has been for protection *from* the athlete who dabbles in drugs. It would be far more effective and on target if our energies were focused on the protection *of* the athlete who faces defensible as well as indefensible uses of drugs. What remains is to tell it the way it really is to athletes and then put one's dogged efforts into the ethics and competence of their leadership.

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Actions—Ovulen acts to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen depresses the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note: Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen is indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia, and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism, and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis and pulmonary embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates in the United States found relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration, and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable. Retrospective studies in Great Britain have shown a statistically significant association between cerebral thrombosis and embolism and the use of oral contraceptives. This has not been confirmed in the United States.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

Since the safety of Ovulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen. Therefore, if such tests are abnormal in a patient taking Ovulen, it is recommended that they be repeated after the drug has been withdrawn for 2 months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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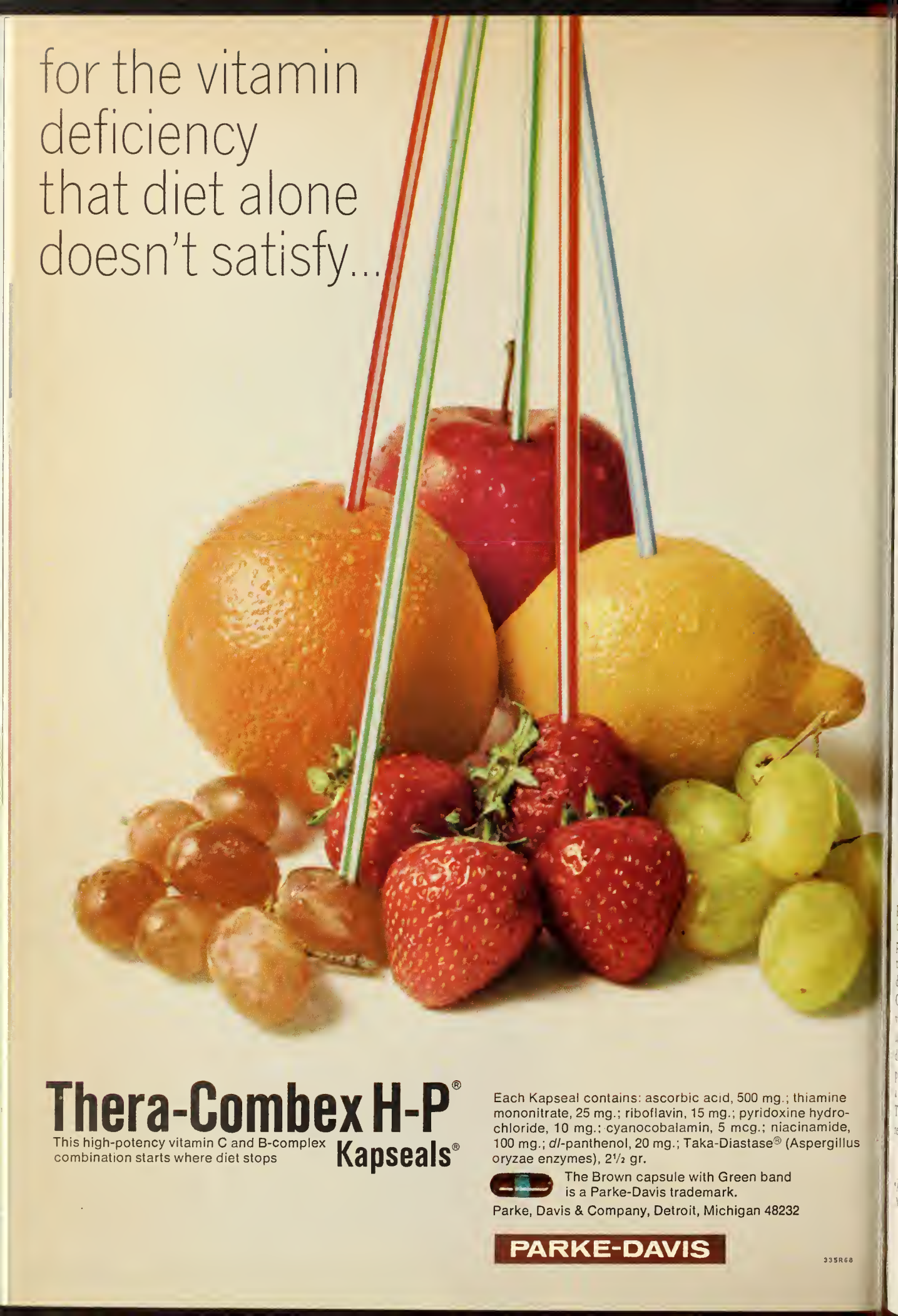
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SPECIAL ARTICLE

The Use of Chlorpropamide in the Treatment of Diabetes Insipidus

HARRY BLOTNER, A.M., M.D.*

Except for posterior pituitary extract given either intramuscularly or intranasally, I have never observed, during my 34 years of studying and treating diabetes insipidus, any practical clinical effect of any hormone or other medication on the fluid intake and output in this disease.[1]

Since 1966, several papers on the beneficial effects of chlorpropamide on the fluid intake and output in diabetes insipidus have appeared from Brazil,[2] Amsterdam,[3] Argentina,[4] and Norway.[5] In the summer of 1968, I found that chlorpropamide could be beneficial in the treatment of diabetes insipidus when I gave it to a patient who had also developed a mild diabetes mellitus and who gained complete relief from his diabetes insipidus. Since then, I have given it orally to four other of my patients and suggested its use for three patients at the Chelsea Naval Hospital, in two of whom the diabetes insipidus followed brain tumor operations.

This paper reports the striking results obtained in certain cases of diabetes insipidus following the oral ingestion of chlorpropamide.

CLINICAL MATERIAL

Five men and three women, ranging in age from 34 to 62 years, were treated. Of my five patients, four have had diabetes insipidus of idiopathic origin for 36 to 43 years, and I have observed them for 32 to 34 years. In the past, many studies had been performed on them.[6–9] The fifth patient has had diabetes insipidus for 16 years, but I had observed her for only five months. These five patients were all ambulatory and were not admitted to the hospital. All had been relieved of their polyuria and polydipsia with the intramuscular administration of Pitressin® tannate in oil or the administration of powdered pituitrin intranasally. The three patients at the Chelsea Naval Hospital included the following: A 38-year-old woman who has had idiopathic diabetes insipidus for 10 years; a 41-year-old man, who had developed diabetes insipidus shortly after the removal of a craniopharyngioma; and a 34-year-old man who shortly after a total hypophysectomy developed diabetes insipidus. The last two had diabetes insipidus for 8 and 15 months respectively.

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CASE REPORTS

Case 1 – F. C., a 62-year-old salesman whose wife and 26-year-old son are living and well. In the past, he had always been well except for the diabetes insipidus.

His daily fluid intake and output, without treatment, had been about 8 to 10 liters. He had been on .5cc of Pitressin tannate in oil intramuscularly (2.5 units of Pitressin tannate) every other day for 26 years. This dose relieved his thirst and polyuria. In most cases of diabetes insipidus, 1 cc. of Pitressin tannate in oil given intramuscularly lasts for 48 hours;[10] in others, it is effective for a little longer or shorter time. Rarely, .5 cc will last for two days.

The physical examination was negative except for the patient's being 25 pounds overweight. On June 24, 1968, a mild diabetes mellitus was found, with a nonfasting blood sugar of 225 mg. and a glycosuria of 4 plus. Although he was placed on a diet of C 150, P 80, and F 80, the diabetes mellitus remained about the same. Because of the coexistence of diabetes mellitus and diabetes insipidus, his appeared to be a very suitable case for treatment with chlorpropamide, and he was started on the drug.

On August 23, 1968, Pitressin tannate in oil was omitted and only chlorpropamide, 250 mg. twice a day, was given. The patient, however, continued to have a marked increase in his fluid intake and output, with frequency in voiding, which greatly interfered with his work as a salesman. On August 26, 1968, he went back to Pitressin tannate in oil, with the usual relief, and simultaneously took chlorpropamide, 250 mg. orally before breakfast and supper. He noted no material difference on chlorpropamide except that the effect of Pitressin tannate in oil lasted longer and he was able to omit Pitressin tannate in oil in 24 days. The daily fluid intake and output dropped to about 1200cc. He had plenty of saliva and no thirst. Fortunately, this patient had an increased blood sugar, for, otherwise, I would not have continued with the chlorpropamide until it had become effective in controlling the diabetes insipidus since it took over three weeks to do so.

The 250 mg. chlorpropamide, which he now takes only once a day provides complete relief from his polyuria and polydipsia. The blood sugars in mid-afternoon continue to range from 90 to 140 mg. The urines remain sugar free with a normal yellow color and with a normal specific gravity.

Case 2 – A. S., a 53-year-old male musician, whose wife and three children are living and well. Without treatment, his daily fluid intake and output have been about 14 liters. Over the past 26 years, he has required the intramuscular administration of 1 cc. of Pitressin tannate in oil every one and one-half to two days in order to keep his polyuria and polydipsia under control. Physical examination showed a height of 66 inches and was not remarkable except for being 35 pounds overweight and a blood pressure of 176/106.

An attempt was made to omit Pitressin tannate in oil and to start chlorpropamide. However, he was unable to do so because the marked increase in the fluid intake and output to about 13 liters interfered with his occupation. Pitressin tannate in oil was resumed, with the usual relief and simultaneously on November 20, 1968, chlorpropamide, 250 mg. twice a day was given. This

time, he noted that the effect of the Pitressin tannate lasted longer. Three weeks later, he discontinued Pitressin tannate in oil, and his daily fluid intake and output were 4 to 4½ liters. It is interesting that his daily intake and output were normal during the day but increased appreciably at night. In April 1969, he went back to the Pitressin tannate in oil because he said that it gave him more relief. For about two years, he has had some social problems and has been drinking about one and one-half quarts of wine daily.

Case 3 – E. K., a 55-year-old school teacher, is married, and her husband and four children are living and well. Her daily fluid intake and output, when she is not treated, have been about 12 liters. During the past 26 years, she has required 1 cc. of Pitressin tannate in oil intramuscularly every other day and occasionally every day in order to keep her daily fluid intake and output normal. She was studied thoroughly during her first pregnancy.[12] The fluid intake and output, which were as high as 13 to 15 liters during that pregnancy, decreased to near normal without treatment shortly before confinement. However, one day post partum, the polyuria and the polydipsia abruptly returned. The subsequent three pregnancies followed a similar pattern, but there was not so marked a decrease in the intake and output at their tremination. She had her menopause three years ago. A nonfasting blood sugar was 120 mg.

Her physical examination was not remarkable. When she omitted the Pitressin tannate in oil, the fluid intake and output were 12 to 13 liters. In November 1968, chlorpropamide, 250 mg. twice a day was started and in 36 hours, her fluid intake and output became normal. She says that she has even better control than while she was on Pitressin tannate in oil. She has been taking chlorpropamide for over six months, and occasionally forgets the evening dose without any change in her intake and output.

Case 4 – K. R., a 34-year-old single, school teacher, has had diabetes insipidus for 16 years. Her daily intake and output, without treatment, are about 8 to 9 liters. She required 1 cc. of Pitressin tannate in oil intramuscularly every two days to control her polyuria and polydipsia. Her menses have been irregular and scant. The physical examination showed her to be obese. Her height was 66½ inches and weight was 305 pounds. The blood pressure was 150/114.

She omitted Pitressin tannate in oil and took chlorpropamide, 250 mg. twice a day with no obvious effect on the intake and output. She went back on Pitressin tannate in oil, and simultaneously took chlorpropamide, 250 mg. twice a day on February 5, 1969. This time, the patient noted that the effect of the Pitressin tannate in oil was lasting longer. Because of her obesity, the dose of chlorpropamide was increased to 250 mg. three times a day, and the effect of the Pitressin tannate in oil was lasting for eight days, a period which at the time appeared quite satisfactory to the patient. Her blood sugar was 110 mg. at 11:00 a.m.

It is interesting that she drank 40 ounces of water from 6:00 a.m. to 6:00 p.m. and the desire to drink increased during the evening. She took about three quarts from 6:00 p.m. to 6:00 a.m. However, she said that she felt better on Pitressin tannate in oil, and consequently the chlorpropamide was omitted. She further noted that she had the taste of the drug from three to four days after its omission.

Case 5 – G. A., a 41-year-old single businessman, has had diabetes insipidus for 33 years. Pitressin tannate in oil intramuscularly had an antidiuretic effect for one and one-half days. However, he preferred powdered pituitrin intranasally 4 to 6 times a day because it gave him satisfactory relief without injection. When he omitted the intranasal pituitrin, his fluid intake and ouput were approximately 14 quarts. He was then given chlorpropamide, 250 mg. daily for a week without appreciable benefit. Resuming pituitrin intranasally afforded him relief. Then chlorpropamide, 250 mg. twice a day, was taken orally for 25 days with intranasal pituitrin. Chlorpropamide did not prolong the effect of the pituitrin. The blood sugar was 130 mg. in the afternoon.

Cases 6, 7 and 8 – The following three patients with diabetes insipidus at the U.S. Naval Hospital, Chelsea, Mass., were treated with chlorpropamide at my suggestion. The results are given here through the courtesy of the Hospital.

Case 6 – Mrs. P., a 38-year-old married woman, has had idopathic diabetes insipidus since 1959. Her husband and five children are living and well. Taking Pitressin tannate in oil intramuscularly every three days relieved the polydipsia and polyuria. In 1964, a radical mastectomy for carcinoma of the breast was performed. In April 1968, she had an oophorectomy for carcinoma of the breast.

She was taken off Pitressin tannate in oil for three days beginning April 14, 1969, and the intake and output of fluid were 5 liters. Then, on April 17, 1969, she was given chlorpropamide, 250 mg. twice a day, and within 48 hours, the daily fluid intake and output dropped to 1500 to 1700 cc. The patient was very pleased with this result. Her blood sugar was 90 mg. fasting and in the afternoon. She is receiving radiation therapy for nodes in the mediastinum. On May 6, 1969, she developed esophagitis with vomiting as a result of x-ray treatment. On one occasion her blood sugar was 54 mg. after lunch. The dose of chlorpropamide was reduced to 250 mg. once a day with the same relief of her fluid intake and output, and her blood sugar is normal.

Case 7 – F. M., a 41-year-old man, developed diabetes insipidus shortly after the removal of a craniopharyngioma in February 1968. His fluid intake and output ranged from 9 to 10 liters for about a year postoperatively although at one time they reached 15 to 16 liters a day. Pitressin tannate in oil intramuscularly controlled the diabetes insipidus but had to be omitted when the patient developed angioneurotic edema and urticaria.

The patient was given chlorpropamide, 250 mg. twice a day, and the fluid intake and output dropped to approximately 6 liters, a decrease which was quite helpful in view of his allergic reaction to the Pitressin tannate in oil. He also took thyroid gr. 3 daily as well as 25 mg. of cortisone in the morning and 125 mg. in the evening.

Case 8 – G. R. F., a 34-year-old naval lieutenant, had acromegaly secondary to eosinophilic adenoma of the pituary gland. On September 12, 1968, a total hypophysectomy was performed resulting in marked improvement of the acromegaly. Shortly thereafter, he developed diabetes insipidus with a fluid intake and output of 6 liters. He was given a trial of chlorpropamide, 250 mg. twice a day, and his intake and output dropped to the 2 to 2.5 liter range. This response took place on the first day.

Discussion

In the eight cases of diabetes insipidus presented in this paper, there was complete relief from the polyuria and polydipsia in four cases, three of idiopathic origin and one following a hypophysectomy for acromegaly secondary to eosinophilic adenoma of the pituitary gland. There was a considerable drop in the fluid intake and output or a prolonged effect of Pitressin tannate in oil in three cases, two of idiopathic diabetes insipidus and one case of diabetes insipidus following an operation for a craniopharyngioma. There was no effect in one case of idiopathic diabetes insipidus.

Apparently, chlorpropamide was first used by Arduino, Ferraz, and Rodrigues.[2] It is interesting how this came about. One of their patients with indiopathic diabetes insipidus took this drug wrongly at his own discretion. He reported such striking effects that the authors investigated the alleged response of the drug in three patients with diabetes insipidus of idiopathic origin and two with diabetes insipidus of nephrogenic origin. In two patients, the urine volume became normal

by the third and fourth days and in a third case the urine volume dropped one-half. In two patients with nephrogenic diabetes insipidus, chlorpropamide was ineffective on the polyuria. There was no hypoglycemia. Frøyshov and Haugen[5] also found chlorpropamide ineffective in nephrogenic diabetes insipidus. Chlorpropamide has been effective in the treatment of diabetes insipidus following hypophysectomy.[5,13]

The mode of the antidiuretic action of chlorpropamide appears to be similar to that of vasopressin by acting on the renal tubule as shown by investigations on patients with diabetes insipidus by Meinders and associates[3] and Reforzo-Membrives and associates.[4] Similar observations in the toad were made by Ingelfinger and Hays[14] who found that chlorpropamide may produce a direct vasopressin-like effect on the renal tubules, or could increase the sensitivity of the tubule to small amounts of vasopressin that may persist in diabetes insipidus.

Chlorpropamide and Pitressin tannate in oil appear to have a similar effect on increasing the salivary secretion. The patients with diabetes insipidus noted that they had an increased amount of saliva when treated with chlorpropamide.

In the past, I studied[11] the volume of saliva secreted following a salivary stimulant in patients with diabetes insipidus before and after treatment with Pitressin. In untreated patients, the salivary output was unusually small ranging from 1.5 to 4.5 cc. during a 15-minute test period. In contrast, after the injection of Pitressin the salivary secretion during the test period increased to volumes ranging from 12 to 25 cc., normal amounts. It is now interesting to find in four patients treated with chlorpropamide that the salivary secretion during the 15-minute test periods ranged from 15 to 22 cc., similar to that found after Pitressin injection.

Other suggestions as to its mode of action are a direct stimulus on the elaboration or release of antidiuretic hormone; a restoration of possibly insensitive osmoreceptive centers to the physiological stimuli, and a direct action on the kidney by the replacement of the antidiuretic hormone. Rarely hypoglycemia may occur in patients with diabetes insipidus taking chlorpropamide when not eating sufficiently. Patients should be advised of this possibility and told how to prevent it. Whatever its mode of action, chlorpropamide appears to be a useful drug in the treatment of diabetes insipidus.

Summary

This paper presents a study of the use of chlorpropamide in the treatment of eight patients with diabetes insipidus, six of idiopathic origin and two following brain surgery. Complete relief from the polyuria and polydipsia was obtained in three cases of idiopathic diabetes insipidus and one due to hypophysectomy. Considerable relief from the polyuria and polydipsia or prolonged effect of the Pitressin tannate in oil occurred in two cases of idiopathic diabetes insipidus and one following a craniopharyngioma operation. There was no effect in one case of idiopathic diabetes insipidus. The effect of the chlorpropamide on the fluid intake and output may take place within 36 hours. The simultaneous administration of chlorpropamide with the intramuscular injection of Pitressin tannate in oil may prolong the effect of the Pitressin tannate in oil considerably after a period of 3 to 4 weeks.

The mode of action of the drug appears in part at least, similar to that of the antidiuretic hormone. Chlorpropamide increases the salivary output and abolishes thirst. Rarely, hypoglycemia may occur in patients with diabetes insipidus taking chlorpropamide when not eating sufficiently. Patients should be advised of this possibility and told how to prevent it. Chlorpropamide appears to be a useful drug in the treatment of diabetes insipidus.

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416 Marlboro Street, Boston, Massachusetts 02115.

Important Dates For Your Calendar

JUNE 1970	Sunday 7	Reserved for **117th ANNUAL SESSION** of the Maine Medical Association at **The Colony** Kennebunkport, Maine Tel. 967-3331
	Monday 8	
	Tuesday 9	

Our Meeting is Moving to The Colony Kennebunkport

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Quinidine

The current therapeutic status of quinidine has changed little since Wenckebach's classic observations on recurrent atrial fibrillation. Although many antiarrhythmic agents have appeared on the pharmacologic horizon, none has surpassed the efficacy of quinidine, an agent effective in any active arrhythmia, whether atrial, A-V nodal or ventricular. The introduction of precordial electroshock therapy by Zoll and his associates and Lown has imparted a new dimension in the approach to antiarrhythmic therapy and made it possible to convert almost 90 percent of the patients with atrial fibrillation to sinus rhythm. Nevertheless, the usefulness of quinidine has not diminished because a pharmacologic program must be instituted to maintain a sinus rhythm even after electroconversion.

The usual drug method of converting atrial fibrillation to sinus rhythm in the digitalized patient is to administer quinidine in a dosage of 0.2 gm every 2 hours for 5 doses the first day; 0.3 gm every 2 hours for 5 doses the second day; 0.4 gm every 2 hours for 5 doses the third day; and so forth. If conversion fails at 0.6 gm (total daily dose of 3.0), the likelihood of conversion is small and the maintenance of sinus rhythm is probably not feasible. Higher doses are attended with toxicity, quinidine syncope, and cardiac standstill. Although quinidine may be useful in converting atrial flutter, the drug should not be used to convert atrial flutter with 2:1 A-V conduction ratio without prior digitalization, since the vagolytic effects of quinidine may allow 1:1 A-V conduction to occur with a dangerously rapid ventricular rate. Quinidine may be administered in a dose of 0.2 to 0.4 gm three to four times a day to control ventricular or atrial premature systoles. Quinidine may be effective in the treatment of arrhythmias associated with Wolff-Parkinson-White syndrome and occasionally it may abolish the electrocardiographic changes of this syndrome. The combination of a small dose of quinidine 100 to 200 mg Q.I.D. with propranolol 10 to 20 mg. Q.I.D. has proved extremely effective in controlling Wolff-Parkinson-White tachycardia, recurrent atrial flutter or fibrillation and in the presence of intermittent ventricular tachycardia.

Although it has been traditionally recommended that a test of quinidine be given to elicit idiosyncrasy, many clinicians utilize the first dose of a therapeutic program for this purpose.

Toxicity may be manifested by pulmonary, gastrointestinal, or cardiac signs and symptoms. Cyanosis, respiratory depression, vascular collapse, restlessness, pallor, cold sweat and syncope are not uncommon. Cinchonism may develop with tinnitus, vertigo, visual disturbances, headache, confusion, angioneurotic edema, nausea, vomiting, diarrhea, fever, or cutaneous manifestations. Thrombocytopenia has been observed occasionally and may be associated with a grave prognosis.

A widening of the QRS complex of more than 25 percent is a warning of impending toxicity and the drug should be discontinued. Cardiotoxicity may be successfully antagonized by 40 to 80 mEq molar sodium bicarbonate or 1 to 3 mg. per minute of isoproterenol.

Procainamide

More than 40 years ago, it was found that procaine could paralyze extracardiac nerves; but, because of rapid hydrolysis, therapeutic levels were difficult to maintain and it never became a clinically useful antiarrhythmic drug. On the other hand, procainamide which binds para-aminobenzoic acid and diethylaminoethanol through an NH group is not affected by the choline esterase of the body and consequently is effective by the oral and parenteral routes with a more prolonged duration of action.

The hemodynamic effects of procainamide are not unlike quinidine. However, large doses of intravenous procainamide may cause serious hemodynamic derangements.

Although it was originally thought that procainamide depressed contractility of cardiac muscle less than quinidine, more recent studies suggest that equivalent doses expressed as milligrams per kilogram depress cardiac muscle equally.

As in the use of quinidine, it is important to realize that patients with renal damage or with congestive heart failure excrete procainamide more slowly than do normal persons, and cumulative effects are a potential danger. Procainamide, like quinidine, acts on the atrium and ventricle by increasing the refractory period and conduction time and has anticholinergic effects on the atria and A-V node. The electrophysiologic effects of the drug are similar to those of quinidine. However, these similarities do not adequately explain the successful use of one drug when the other has failed as an antiarrhythmic agent.

Although procainamide is probably less successful than quinidine in reverting atrial fibrillation to sinus rhythm, it has been used in quinidine-sensitive patients. Likewise, it has been effective in restoring sinus rhythm in patients with atrial flutter and atrial tachycardia. Procainamide appears to have a distinct advantage over quinidine in the management of ventricular tachycardia, when urgent intravenous therapy is required. The rate of intravenous administration should not exceed 100 mg per minute, and electrocardiographic monitor-

ing is imperative during the period of injection. We have frequently and successfully treated atrial tachycardia with block and ventricular tachycardia, with procainamide in the presence of digitalis overdosage. However, the management of ventricular or junctional tachycardia in high grade A-V block requires special attention. Depressant agents, such as quinidine, procainamide and potassium salts may abolish all subsidiary pacemakers and engender cardiac standstill. Hence, electrical pacing or isoproterenol are best utilized in this clinical setting.

The toxic signs of procainamide include hypersensitivity reactions such as skin eruptions, bone marrow depression, or lupus erythematosus with proteinuria and polyserositis. The development of hypotension or widening of the QRS complex beyond 25 percent of control is a definite indication to withdraw this agent. As in the use of quinidine, infusion of hypertonic sodium salts will reverse procainamide toxicity.

Lidocaine

The pharmacologic activity and electrophysiologic mechanisms of lidocaine are similar to quinidine and procainamide. It has proved extremely effective in terminating ventricular tachycardia, especially in the presence of an acute myocardial infarction and premature ventricular systoles.

The main hallmark of this agent is its superiority to procainamide in certain specific situations when a short-acting agent is required, particularly in hearts previously depressed by other antiarrhythmic agents or where only a transitory antiarrhythmic effect is indicated. It has been used successfully in depressed hearts following open heart surgery to control ventricular tachycardia prior to the termination of extracorporeal circulation. However, it is impractical for the very long-term treatment or prevention of paroxysmal ventricular tachycardia. It is safe and effective in a single intravenous dose of 1 mg per kilogram with repeated doses every 20 minutes to a maximum of 750 mg. Usually a bolus injection of 50 to 100 mg is administered intravenously followed by an intravenous drip of 2 to 4 mg per minute to prevent the reappearance of ventricular premature systoles. This agent has significantly reduced the mortality associated with ventricular tachycardia and fibrillation in the presence of an acute myocardial infarction and has become the most useful antiarrhythmic agent in the coronary care unit. Similar restrictions as stated under quinidine and procaine should be observed in the presence of high grade A-V block.

Diphenylhydantoin

Diphenylhydantoin (Dilantin®) appears equally effective in both supraventricular and ventricular arrhythmias and possesses properties which make it effective against digitalis-induced arrhythmias. It has been successful in preventing paroxysmal atrial tachycardia (PAT) when the usually employed antiarrhythmic agents have failed. It has proved effective in suppressing atrial, A-V nodal, and ventricular premature systoles, and is particularly effective in terminating digitalis-induced arrhythmias. Its transient action and rapid reversibility of toxic effects may give it certain advantages over other depressant agents. However, it does not appear effective in converting atrial fibrillation to sinus rhythm. In the treatment of rapid supraventricular or ventricular tachycardias, 5 to 10 mg per kilogram can be slowly injected intravenously over a 15 minute period and repeated within 2 to 3 hours. The drug can be administered orally, from 100 to 200 mg four times daily, for the suppression of ectopic beats or prophylaxis against recurrent paroxysmal tachycardia.

Toxic manifestations of diphenylhydantoin are seen in approximately 10 to 15 percent of patients and include nervousness, ataxia, tremors, nystagmus, visual disturbances, respiratory arrest, confusion or drowsiness, gastric distress, erythematous or morbilliform cutaneous eruptions and hyperplasia of the gums.

Beta Adrenergic Blocking Agents

Interest in blocking the effects of adrenergic nerve stimuli is attributed to Dale who, in 1906, described the reversal of the pressor response to epinephrine by pretreating experimental animals with certain ergot compounds. Alhquist recognized two types of adrenergic receptors and designated these alpha and beta.

Propranolol reduces the heart rate and cardiac contractile force. Arterial pressure and ascending aortic flow are slightly reduced in anesthetized dogs. As these changes do not occur after depletion of norepinephrine stores by syrosingopine, it is concluded that they result from blockade of resting sympathetic drive. In humans, administration of propranolol will cause a decrease in cardiac output and left ventricular work at rest and during exercise. Propranolol will abolish the vasodilation effects of epinephrine and isoproterenol but not the vasoconstrictor effects of tne catecholamines on the peripheral vessels.

With intravenous administration, propranolol exerts a rapid antiarrhythmic action. Propranolol is usually given slowly in doses of 1 to 5 mg intravenously, (no more than 1 mg every 2-3 minutes) or 15 to 30 mg three to four times daily may be given by the oral route prophylactically to prevent the return of ectopic beating. The action is usually immediate during the intravenous administration and the drug may be repeated within 2 to 3 hours.

The side effects of propranolol may include lightheadedness, drowsiness, nausea, diarrhea, sleeplessness, rashes, visual disturbances, purpura, paresthesias, flushing, and mental confusion. The pharmacologic effects of propranolol have produced hypotension, bradycardia, cardiac failure, A-V heart block, bronchial wheezing and aggravation of mild obstructive pulmonary disease.

Submitted by Jacob B. Dana, M.D., Maine Heart Association

County Society Notes

PENOBSCOT

A meeting of the Penobscot County Medical Society was held on November 18, 1969 at the West Hampden Country Club in Hampden, Maine with Lloyd Brown, M.D., President, presiding.

The guest speaker, Daniel F. Hanley, M.D., Executive Director of the Maine Medical Association, gave a most interesting talk on his experiences with athletes in the Olympiads. He emphasized the strong competitive drive in athletes, enabling them to compete with injuries which, under ordinary circumstances, would be severely limiting. He also discussed the doping problem and methods of screening athletes for doping and sex determination. His talk was well received by the audience of fifty physicians.

At the business meeting which followed, there was brief discussion of the Implied Consent Law. This law is receiving intensive study by many groups and the Ad Hoc Committee had no specific resolution to present at this time.

Robert P. Andrews, M.D. reminded the group that he has a list of re-education courses available and that these courses are under RMP sponsorship.

Lloyd Brown, M.D. announced a nominating committee to bring in a slate of officers at the annual meeting in December: Chairman, Jay K. Osler, M.D., William A. Purinton, M.D. and Leonard G. Miragliuolo, M.D.

WILLIAM M. SHUBERT, M.D., *Secretary*

HANCOCK

The annual meeting of the Hancock County Medical Society was held on December 10, 1969 in Ellsworth, Maine with thirteen members and four guests present.

The assembly heard remarks by the Maine Medical Association President, Charles F. Branch, M.D., a guest at the meeting. The minutes of the previous meeting were read and approved.

Nominations for officers in the County Society were approved as follows:

President, Randall H. Silver, M.D., Ellsworth
Vice-President, Robert C. Granger, M.D., Blue Hill
Secretary, Bradley E. Brownlow, M.D., Blue Hill
Delegates to the M.M.A. House of Delegates, Drs. Richard W. Britt, Blue Hill and Eliot T. Stadler, West Goulds-boro. Alternates, Drs. Charles H. Knickerbocker and Winston G. Stewart, both of Bar Harbor
Censors, Drs. Walton P. C. Clason, Ellsworth, Robert C. Granger, Blue Hill and Robert D. Wilson, Bar Harbor

An address entitled "Childhood Seizure Disorders, Classification and Treatment" was given by John C. Van Pelt, M.D. of Ellsworth.

BRADLEY E. BROWNLOW, M.D., *Secretary*

LINCOLN-SAGADAHOC

A meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on December 16, 1969. The meeting was called to order by the President, Paul A. Fichtner, M.D.

The only old business was the donation to the Caddies' fund. Since both Drs. Frank O. Avantaggio, Jr. and Francis A. Winchenbach were absent, Dr. Carl R. Griffin, Jr. moved that the decision regarding an amount be postponed to the January meeting and the motion was unanimously passed.

John F. Andrews, M.D. reported on the last meetings of the Council of the Maine Medical Association. The major thought to be presented now was the status of doctors of osteopathy vis-a-vis the M.M.A. John F. Dougherty, M.D. suggested that further study be made of this subject prior to instructing the delegates. Dr. Andrews mentioned the question of student category of membership in the M.M.A. as there are ninety-five students from this State currently in medical schools; the fact that some contaminated kits of Bard catheters are spread throughout the State; and urged members to join MEMPAC. He stressed that the U. S. Department of Health and Welfare is interested in a rubella vaccination campaign. Drs. Mary J. Tracy and Charles E. Burden were appointed a committee to study the campaign and report on this to the next meeting.

Dr. Fichtner appointed Drs. John F. Dougherty, Samuel L. Belknap and John F. Andrews to the nominating committee to bring in a proposed slate of officers for the Society elections at the January meeting.

Henry A. Hudson, M.D. introduced the guest speaker, Raymond H. Dominici, M.D. of the Maine Medical Center in Portland. Dr. Dominici spoke about snowmobile injuries.

GEORGE W. BOSTWICK, M.D., *Secretary*

KENNEBEC

The annual meeting of the Kennebec County Medical Association was held at the Augusta State Hospital in Augusta, Maine on December 11, 1969. Members and guests were welcomed by John C. Patterson, M.D., Director of the Augusta State Hospital. Following an excellent dinner, the business meeting was convened by Joseph R. Crawford, M.D., President. The Secretary's report was read and accepted. The Treasurer's report was deferred until the January meeting.

A communication was read from Mrs. Terrance Sheehan, Chairman, Health Careers, Kennebec County Medical Society Auxiliary requesting that our Society donate $250.00 to the purchase of a slide program and synchronized tape narration material and equipment to show this Health Careers material. It was voted that this matter be referred to the Council for further discussion.

Hugh J. Mathews, Jr., M.D. presented a resolution on the death of Kurt A. Sommerfeld, M.D. and the Secretary read a resolution on the death of Edwin A. Harlow, M.D.

The report of the nominating committee was presented by Kenneth E. Smith, M.D. On a motion by Brinton T. Darlington, M.D., it was moved that nominations be closed and the Secretary cast one vote for the slate of officers as nominated and this was done.

The following officers and delegates to the Maine Medical Association for 1970 are:

President, George I. Gould, M.D., Richmond
Vice-President, Paul A. Jones, Jr., M.D., Waterville
Secretary-Treasurer, Francis A. Spellman, M.D., Togus
Councilors, Drs. Richard R. Dole, M.D., Waterville (3 yrs.), Francis J. O'Connor, Augusta (2 yrs.) and John C. Patterson, Augusta (1 yr.)
Delegates to the M.M.A. House of Delegates, Drs. Brinton T. Darlington, Allan J. Stinchfield and John C. Patterson, all of Augusta; Earle M. Davis and Valentine J. Moore, both of Waterville; and Alfredo Monsivais, Winthrop. Alternates, Drs. Theodore M. Russell, John H. Shaw and John D. Denison, all of Augusta; Richard T. Chamberlin and Richard L. Chasse, both of Waterville; and Richard E. Barron, Winthrop

Note was made that the present delegates were elected for a term of two years in January of 1969. Present election was to serve as a reminder to the membership of who their delegates are. It was agreed that Committees would be appointed at the next Council meeting.

Dr. Crawford introduced the speaker of the evening, Verne Caviness, M.D. of the Department of Neuropathology at Harvard

Medical School. Dr. Caviness discussed Epilepsy following Head Trauma and reviewed in a fascinating manner a statistical analysis of WWI post traumatic epilepsy experience. In the post program discussion period, Dr. Caviness touched upon other current subjects such as low pressure hydrocephalus.

Prior to adjournment, Dr. Crawford introduced the new President, George I. Gould, M.D., who adjourned the meeting.

FRANCIS A. SPELLMAN, M.D., *Secretary*

CUMBERLAND

A meeting of the Cumberland County Medical Society was held on December 18, 1969 at the Stage Coach Restaurant in South Portland, Maine. After the usual social hour, an excellent dinner was enjoyed by sixty-five members and guests. A special vote of thanks was given to Mr. Don Larue of the Stage Coach Restaurant for his excellent cooperation in making this meeting possible.

The business meeting was called to order by the President, George F. Sager, M.D. and it was voted that the reading of the minutes of the last meeting be omitted.

The application of Richard L. White, M.D., accompanied by a letter of transfer, was read to the Society and it was voted that he be accepted into membership.

Robert F. Ficker, M.D., District Representative, was introduced and he brought to the attention of the Society matters relating to the Council of the Maine Medical Association.

Reports were presented by the following committees:

1. Public Relations
2. Legislative Affairs
3. Program
4. Utilizations of Extended Care
5. Medical Careers
6. Medical-Legal Liaison
7. Diabetic Detection
8. State Health Insurance (No report)
9. Committee on the Search for City Health Physician
10. Bylaws
11. Southern Maine Comprehensive Health Association, Inc.

Reports of these committees which were accepted are to be printed and distributed to the Representatives of the Council and the State Executive body.

The chairman of the nominating committee, Eugene P. McManamy, M.D., gave the report of his committee:

1. Appointment of ten delegates and ten alternates to represent the County Society at the interim and annual meetings of the House of Delegates of the Maine Medical Association in 1970 was as listed:

Delegates, Drs. George F. Sager and Marvin C. Adams, both of Portland, Paul V. Davis, Bridgton and Houghton M. White, Brunswick (2 yrs.); Drs. David K. Lovely, Stephen E. Monaghan and John F. Gibbons, all of Portland, Ralph F. Turgeon, Westbrook, Kirk K. Barnes, Brunswick and Edmund W. Hardy, Falmouth (1 yr.). Alternates, Drs. Douglass C. Pennoyer, Domenico A. Santoro and Richard C. Dillihunt, all of Portland, and Winton Briggs, Cape Elizabeth (2 yrs.); Drs. Howard P. Sawyer, Jr., Charles E. Skillin and Alfred E. Swett, all of Portland, Robert H. Pawle, Falmouth, Harold N. Burnham, Gorham and Harris Hinckley, South Portland (1 yr.)

2. Slate of Officers:

President, George F. Sager, M.D., Portland
Vice-President, Lawrence Crane, M.D., Portland
Secretary-Treasurer, Douglas R. Hill, M.D., South Portland

It was voted by the Society to accept the slate of officers.

It was noted as an omission that it will be necessary to have the Nominating Committee name one member for a three-year term on the Executive Committee Council.

Notice was given of the January meeting to be held at the Sheraton-Eastland Hotel, January 23, 1970.

DOUGLAS R. HILL, M.D., *Secretary*

ANDROSCOGGIN

The annual meeting of the Corporators of the Androscoggin County Medical Association was held at St. Mary's General Hospital in Lewiston, Maine on December 18, 1969. The meeting was called to order by the President, John W. Carrier, M.D. with seventeen members present.

Lionel R. Tardif, M.D. introduced Mr. Alcide Nadeau who was to give a brief introduction to Model Cities Drug Program. He discussed Federal Funds available to defray the cost for people who can't afford to pay, participants not necessarily of welfare status but low income groups. Complete details are not all worked out as yet. They are trying to get a committee of 1 M.D., 1 pharmacist, 2 laymen and Mr. Thibodeau and hope to start April 1st. The Model City residents are only eligible to participate.

Lillian M. Hall, M.D. of Lewiston was elected to membership in the Association.

Otis B. Tibbetts, M.D. reported for the Finance Committee and the report was accepted.

Stanley D. Rosenblatt, M.D. presented the following slate of officers for the coming year which was accepted:

President, Lionel R. Tardif, M.D., Lewiston
Vice-President, Charles W. Steele, M.D., Lewiston
Secretary-Treasurer, Donald L. Anderson, M.D., Lewiston
Councilor, Lawrence A. Nadeau, M.D., Lewiston
Delegates to the M.M.A. House of Delegates, Drs. Lionel R. Tardif and John W. Carrier, Lewiston. Alternates, Drs. Charles W. Steele, Cyprien L. Martel, Jr. and J. Paul Nadeau, all of Lewiston

Dr. Carrier turned over the chair to Dr. Tardif. Dr. Carrier was given a rising vote of thanks for his services over the past year.

DONALD L. ANDERSON, M.D., *Secretary*

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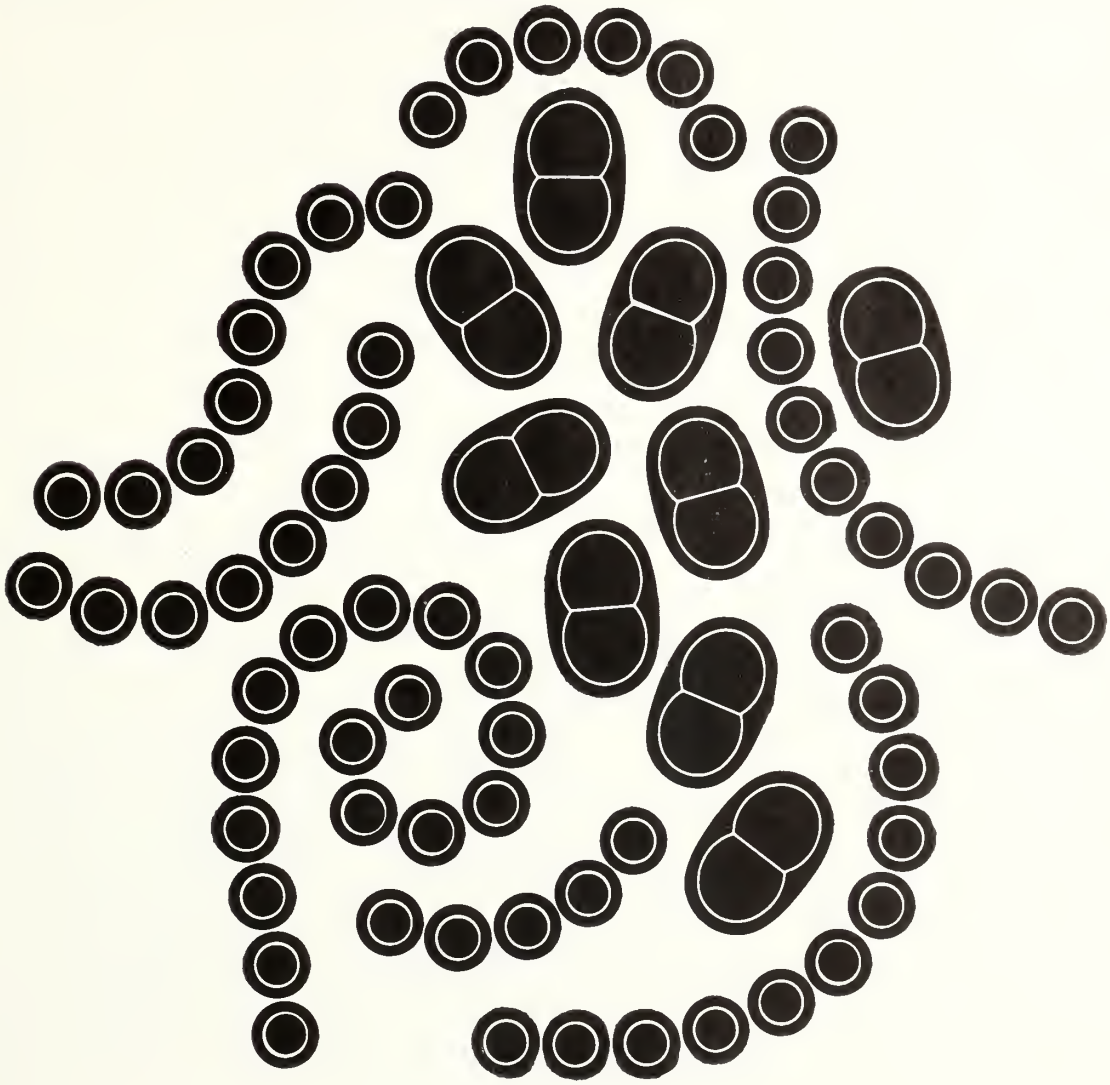

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General Adverse Effects: Because of the high potency of the drug and the variability of its potential to cause adverse reactions, the following are strongly recommended: 1) the lowest possible effective dose for the individual patient should be prescribed. Increased dosage tends to increase adverse effects, particularly in doses over 150-200 mg/day, without corresponding clinical benefits; and 2) careful instructions to, and observations of, the individual patients are essential to the prevention of serious and irreversible, including fatal, adverse reactions, especially in the aging patient.

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Contraindications: Children 14 years of age and under; pregnant women and nursing mothers; active gastrointestinal lesions or history of recurrent gastrointestinal lesions; allergy to aspirin and indomethacin.

Warnings: *Gastrointestinal Effects:* Because of the occurrence and, at times, severity of gastrointestinal reactions, be continuously alert for any sign or symptom signaling a possible gastrointestinal reaction. The risks of continuing therapy with INDOCIN in the face of such symptoms must be weighed against the possible benefits to the individual patient. Gastrointestinal effects may be reduced by giving the drug immediately after meals, with food, or with antacids. Use greater care in aging patients.
Ocular Effects: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients on prolonged therapy. Discontinue therapy if such changes are observed. Ophthalmologic examination at periodic intervals is desirable in patients on prolonged therapy.
Central Nervous System Effects: INDOCIN (Indomethacin, MSD) may aggravate psychiatric disturbances, epilepsy, and parkinsonism, and should be used with considerable caution in patients with these conditions. If severe CNS reactions develop, discontinue the drug.

Precautions: Blurred vision may be a significant symptom that warrants a thorough ophthalmologic examination. Patients should be cautioned about engaging in activities requiring mental alertness and motor coordination, as driving a car. Headache which persists despite dosage reduction requires complete cessation of the drug. May mask the usual signs and symptoms of infection; therefore, the physician must be continually on the alert for this and should use the drug with extra care in the presence of existing controlled infection. After the acute phase of the disease is under control, an attempt to reduce the daily dose should be made repeatedly until the patient is off entirely.

Adverse Reactions: *Gastrointestinal Reactions:* Single or multiple ulcerations of the esophagus, stomach, duodenum, or small intestine, including perforation and hemorrhage, with fatalities in some instances; gastrointestinal bleeding without obvious ulcer formation; perforation of preexisting sigmoid lesions (diverticulum, carcinoma, etc.); rarely, increased abdominal pain in ulcerative colitis patients or development of ulcerative colitis and regional ileitis; gastritis, which may persist after the cessation of the drug; nausea, vomiting, anorexia, epigastric distress, abdominal pain, and diarrhea.
Eye Reactions: Corneal deposits and retinal disturbances, including those of the macula, have been observed on prolonged therapy; blurring of vision.
Hepatic Reactions: Rarely, toxic hepatitis and jaundice, including some fatal cases.
Hematologic Reactions: Aplastic anemia, hemolytic anemia, bone marrow depression, agranulocytosis, leukopenia, and thrombocytopenic purpura. Since some patients manifest anemia secondary to obvious or occult gastrointestinal bleeding, appropriate blood determinations are recommended.
Hypersensitivity Reactions: Acute respiratory distress, including dyspnea and asthma; angiitis; pruritus; urticaria; angioedema; skin rashes.
Ear Reactions: Hearing disturbances, deafness, tinnitus.
Central Nervous System Reactions: Psychotic episodes, depersonalization, depression, coma, convulsions, peripheral neuropathy, drowsiness, mental confusion, lightheadedness, dizziness, headache.
Cardiovascular-Renal Reactions: Edema, elevation of blood pressure, hematuria.
Dermatologic Reactions: Loss of hair, erythema nodosum.
Miscellaneous: Rarely, vaginal bleeding, hyperglycemia, glycosuria, ulcerative stomatitis, and epistaxis.

Supplied: Capsules containing 25 mg indomethacin each, in bottles of 100 and 1000; capsules containing 50 mg indomethacin each, in bottles of 100.

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Each fluidounce contains: 80 mg. Benadryl® (diphenhydramine hydrochloride), Parke-Davis; 12 grains ammonium chloride; 5 grains sodium citrate; 2 grains chloroform; 1/10 grain menthol; and 5% alcohol. An antitussive and expectorant for control of coughs due to colds or of allergic origin, BENYLIN EXPECTORANT is the leading cough preparation of its kind. BENYLIN EXPECTORANT tends to inhibit cough reflex ...soothes irritated throat membranes. And its not-too-sweet, pleasant raspberry flavor makes BENYLIN EXPECTORANT easy to take.
PRECAUTIONS: Persons who have become drowsy on this or other antihistamine-containing drugs, or whose tolerance is not known, should not drive vehicles or engage in other activities requiring keen response while using this preparation. Hypnotics, sedatives, or tranquilizers if used with BENYLIN EXPECTORANT should be prescribed with caution because of possible additive effect. Diphenhydramine has an atropine-like action which should be considered when prescribing BENYLIN EXPECTORANT.
ADVERSE REACTIONS: Side reactions may affect the nervous, gastrointestinal, and cardiovascular systems. Drowsiness, dizziness, dryness of the mouth, nausea, nervousness, palpitation, and blurring of vision have been reported. Allergic reactions may occur.
PACKAGING: Bottles of 4 oz., 16 oz., and 1 gal.
Parke, Davis & Company, Detroit, Michigan 48232
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His heart tells him he's an invalid.
You know he's not.

Photograph professionally posed.

Contraindications: History of sensitivity to meprobamate.

Important Precautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis,

badubdub lubadı

iety is expected in the cardiovascular patient.
tle may even be desirable.

when anxiety is exaggerated . . . when it
feres with sleep . . . when it aggravates
liovascular symptoms, your help may
eeded.

urally, you'll want to reassure the patient.

perhaps prescribe Equanil (meprobamate)
djunctive therapy. It helps relieve anxiety
tension specifically, yet gently.

ost 15 years' use has shown that Equanil
sually well tolerated as well as effective.
effects are generally limited to transient
siness; serious, therapy-interrupting
effects are rare.

stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia usually transient, have been reported on continuous administration.

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely. After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies. Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep; reduction of blood pressure, pulse and respiratory rates to basal levels; and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated.) Doses above 2400 mg./day are not recommended.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. (All tablets also available in REDIPAK® [strip pack], Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

Wyeth Laboratories Philadelphia, Pa.

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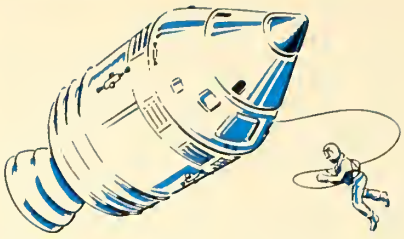
(meprobamate) Wyeth®



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Forte tablets help to relieve pain, mobility . . . stop pain-spasm feedback

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Contraindications: Sensitivity to either component. ***Precautions:*** Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped. ***Adverse Reactions:*** Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, *Paraflex* (chlorzoxazone) may possibly have been associated with gastrointestinal bleeding. While *Paraflex* (chlorzoxazone) and chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately eighteen patients, it was not possible to state that the dysfunction was or was not drug induced. ***Usual Adult Dosage:*** Two tablets q.i.d. ***Supplied:*** Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.*: Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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OF THE

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(Herein Called A H S)

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Certificate of Coverage for Physicians' Service Benefits

This is to Certify: That the Subscriber and Family Members, if any, named on the Subscriber's Identification Card issued as a part of this Contract, are entitled to benefits in accordance with the terms, conditions and provisions appearing hereinafter and made a part hereof.

In Witness Whereof Associated Hospital Service of Maine (a Non-profit Maine Corporation) has duly executed this Contract.

Countersigned by:

President

Chairman of the Board

PHY[illegible] SE[illegible]

Article I [illegible]

Fees For In-Hospital Calls And Surgery

Q. Can more than one physician be paid for in-hospital medical calls on the same day?

A. No.

Q. Can one physician be paid for both in-hospital medical calls and surgery?

A. Many times he can, depending upon the length of stay and whether minor or major surgery is involved. If minor, 4 calls are included in the surgical fee; if major, 21 calls are included. Calls beyond these includable 4 and 21 visits can be paid. If you have a question as to what will be paid, the simplest approach is to indicate on the claim all services rendered. Maximum benefits will then be paid by Blue Shield.

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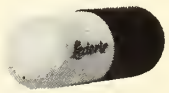
tularemia
typhus fever
urethritis

...don't you think it's time we were on a first-name basis?

call me "Achro® V"



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Contraindications: Hypersensitivity to tetracycline.
Warning: In renal impairment, since liver toxicity is possible, lower doses are indicated; during prolonged therapy consider serum level determinations. Photodynamic reaction to sunlight may occur in hypersensitive persons. Photosensitive individuals should avoid exposure; discontinue treatment if skin discomfort occurs.
Precautions: Nonsusceptible organisms may overgrow; treat superinfection appropriately. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).
Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage. Upon adverse reaction, stop medication and treat appropriately.

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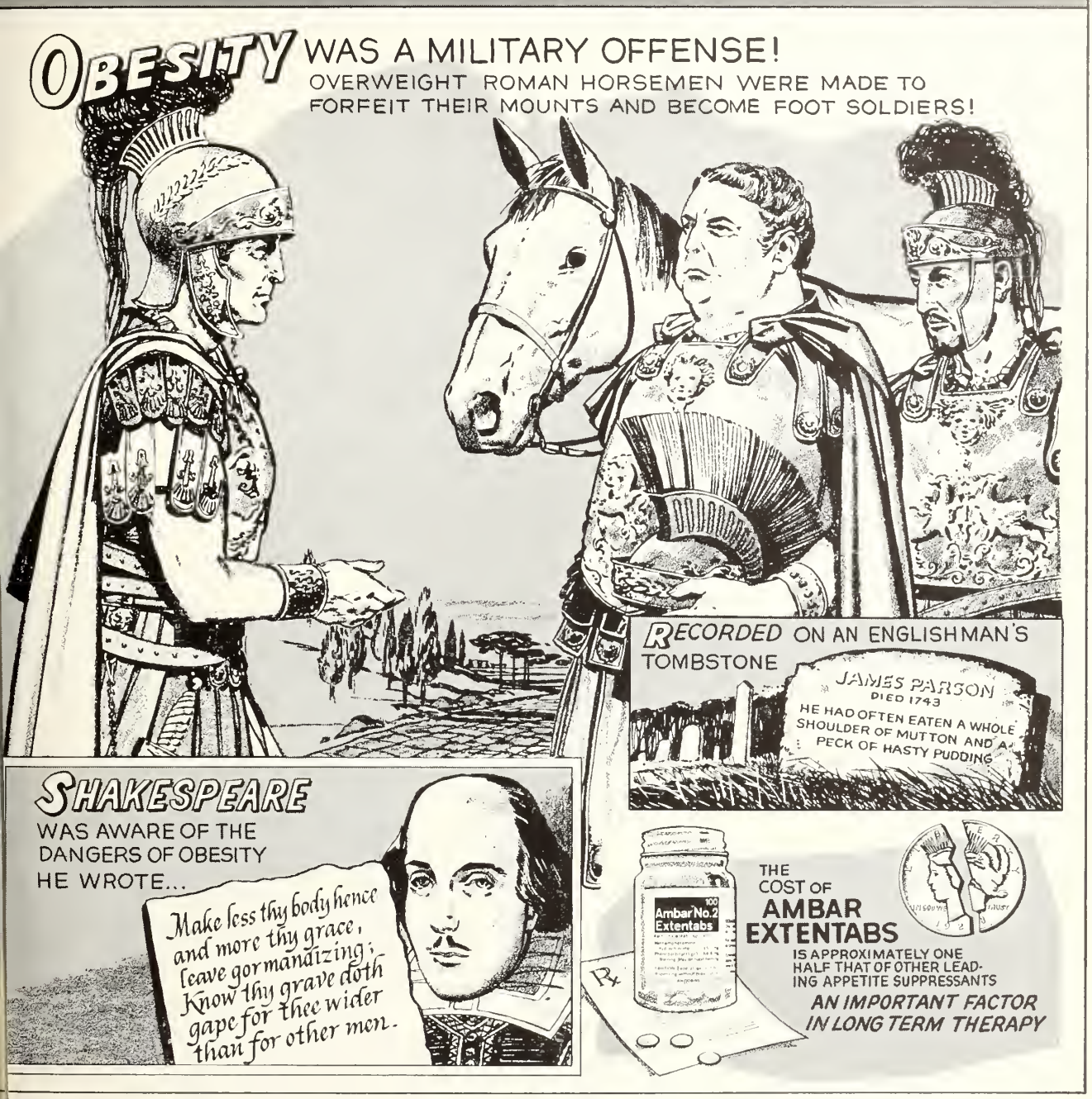

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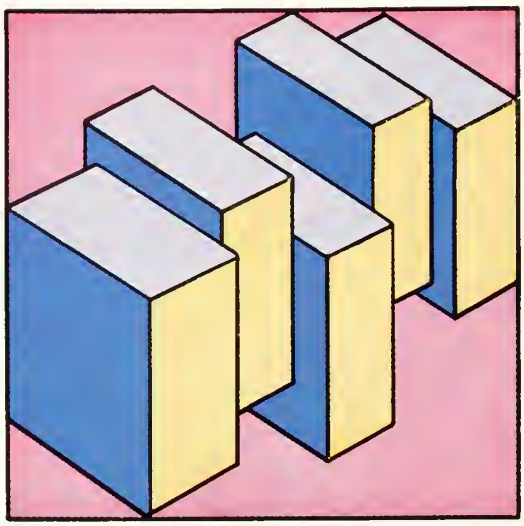
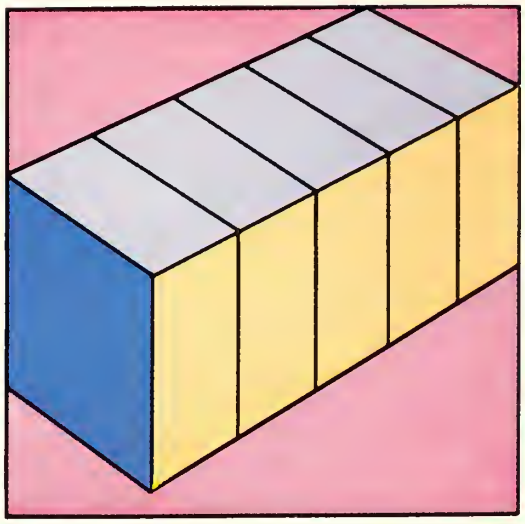


from the discord of anxiety...



to emotional harmony

Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.
CONTRAINDICATIONS: Patients with known hypersensitivity to the drug.
WARNINGS: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.
PRECAUTIONS: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.
ADVERSE REACTIONS: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido--all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause *CNS effects* such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptic an increase in convulsive episodes has been reported. Sympathomimetic cardio*vascular effects* reported include ones such as tachycardia, precordial pain arrhythmia, palpitation, and increased blood pressure. One published repo described T-wave changes in the ECG of a healthy young male after ingestion c diethylpropion hydrochloride; this was an isolated experience, which has not bee reported by others. *Allergic phenomena* reported include such conditions as rash urticaria, ecchymosis, and erythema. *Gastrointestinal effects* such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported Specific reports on the hematopoietic system include two each of bone marro depression, agranulocytosis, and leukopenia. A variety of miscellaneous advers reactions have been reported by physicians. These include complaints such as dr mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decrease libido, dysuria, and polyuria

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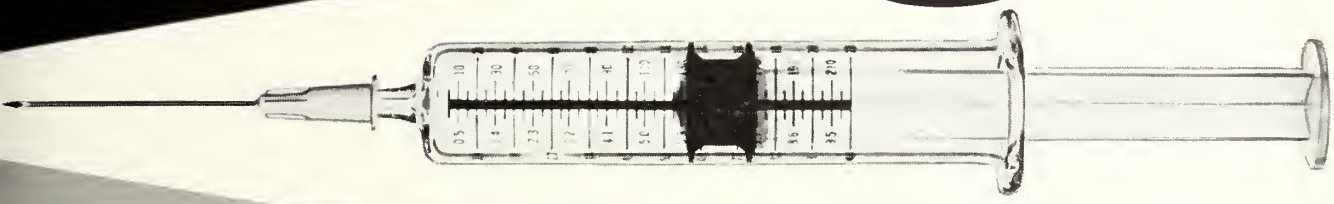

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* ESTHER M. KENNARD, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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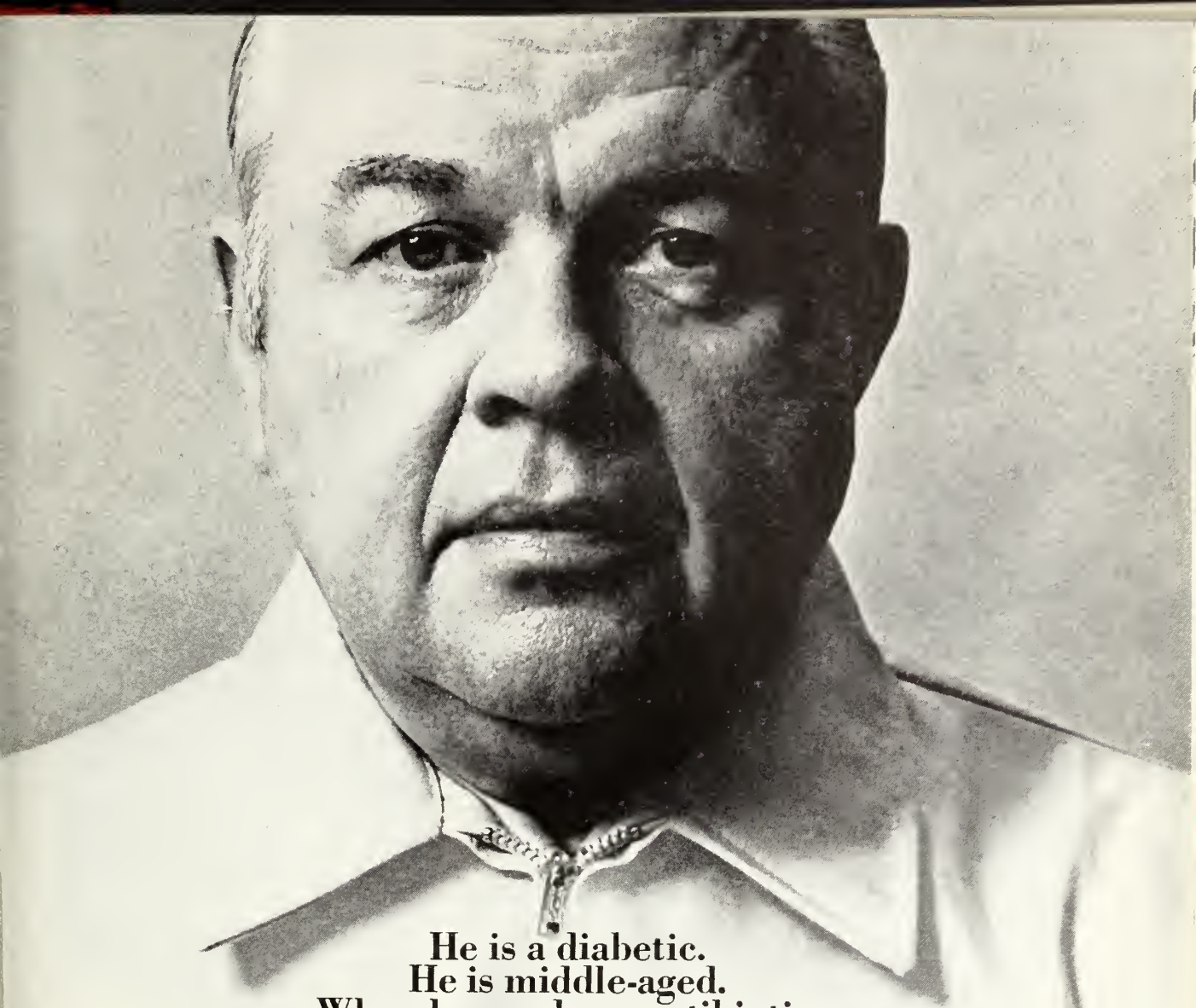

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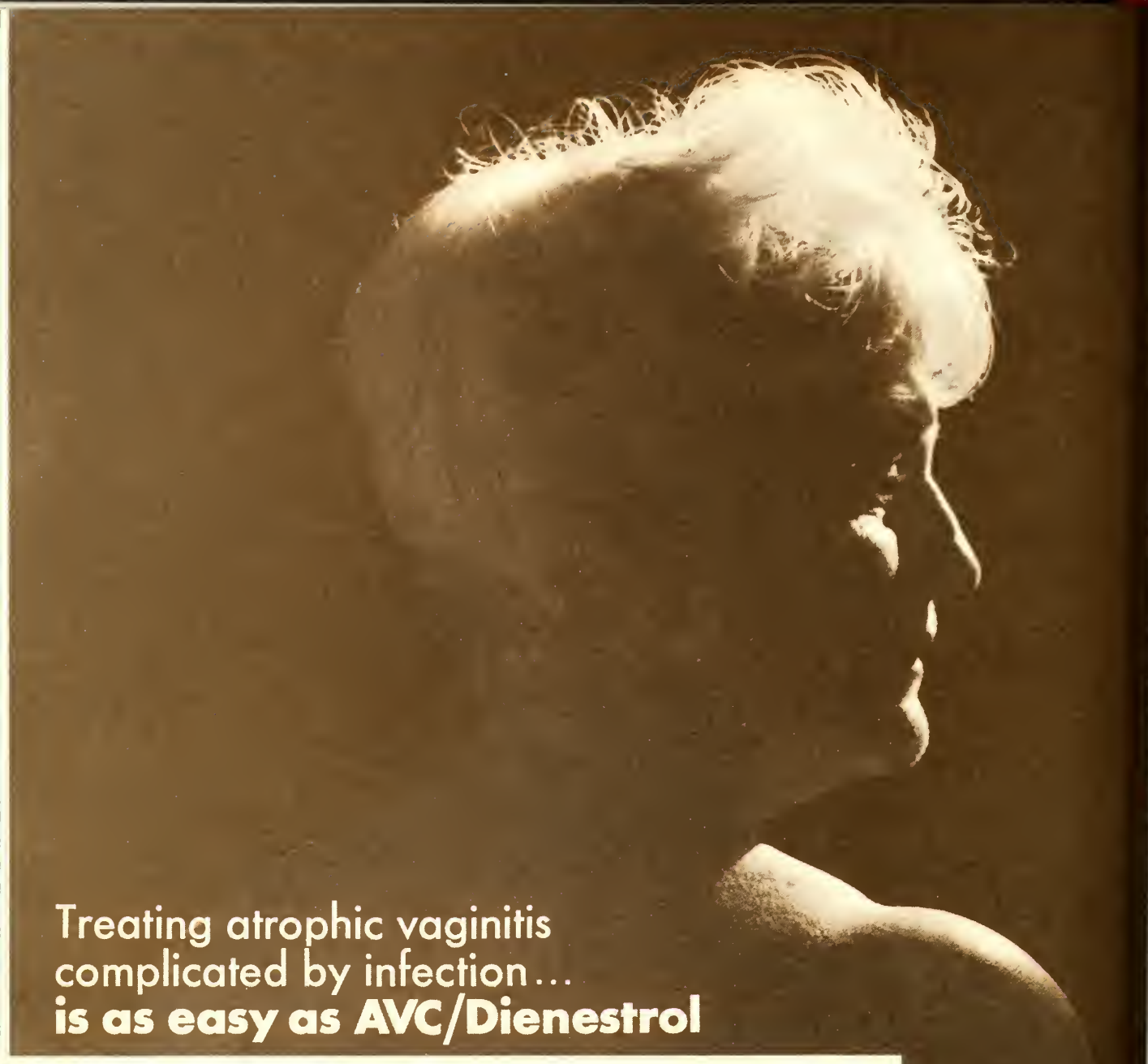

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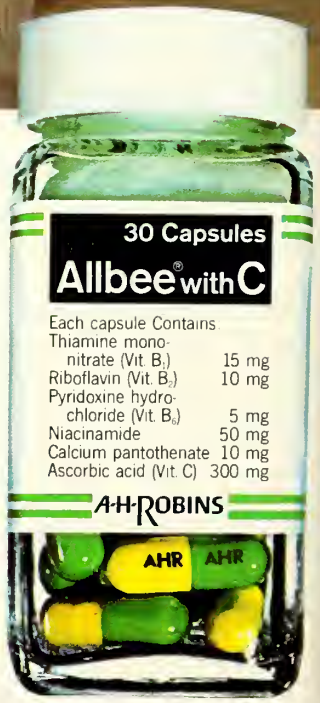

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Volume Sixty-one | Brunswick, Maine, April 1970 | Number 4

Definitive Gastric Surgery in a Small Community Hospital

W. Edward Jordan, Jr., M.D.

With the passage of time, accepted therapeutic techniques tend to migrate from the Medical Center to the Community Hospital. The results obtained at the periphery of definitive medical care constitute a measure of the value of the procedure. I would like to present my experiences in performing 35 definitive gastric operations for a variety of disease states between 1958 and 1968 in a small community hospital.

The diagnoses are listed in Table I. When the patient had both gastric and duodenal ulcer, the latter was considered to be the primary disease and gastric ulceration a secondary phenomena resulting from antral stasis.[1]

The operations are shown in Table II. During the early years of the study, gastrectomy was the preferred treatment of duodenal ulcer but the increasingly favorable reports in the literature of vagotomy and drainage[2] caused a change in this opinion. Vagotomy and drainage was used more frequently in the past five years and represents an improvement in the technique. In general, when vagotomy and drainage was elected, pyloroplasty was preferred over gastroenterostomy,[3] but at times the pylorus was too scarred and edematous to permit this. In these cases, a posterior gastroenterostomy (P.G.E.) was performed with the stoma well down into the antral portion of the stomach. A short afferent limb was employed.

The indications for surgery are shown in Table III. As with most series, intractability was the most common indication. Intractability was considered to be present when the patient had severe symptoms unrelieved by an adequate medical regime over a period of years. Loss of time from work was an important consideration. Patients with gastric ulcer which failed to heal, recurred on a medical regime, or which showed roentgenological signs of malignancy, were subjected to gastric resection.

Preoperative preparation of these patients was considered of great importance. Most published series show a mortality rate connected with the handling of the difficult duodenal stump problem. In order to try and avoid this, the patients were hospitalized a week prior to surgery and maintained on a strict sippy diet. Surgery was performed only after as much medical improvement as it was possible to obtain was indeed present. If an inflamed and edematous duodenum was encountered in spite of these precautions, every attempt was made to avoid resection. In only two cases was a really difficult duodenal stump therefore encountered. Both of these patients had combined gastric and duodenal ulcer, and I felt resection was unavoidable. The first of these developed a pancreatic fistula which closed spontaneously and the second was treated with a cathe-

Table I

Diagnosis	
Duodenal ulcer	20
Duodenal and Gastric ulcer	5
Benign Gastric ulcer	7
Gastric Carcinoma	3
	35

Table II

Operation	
Resection, Bilroth I	10
Resection, Bilroth II	14
Hemigastrectomy and vagotomy	2
Vagotomy and pyeloroplasty	7
Vagotomy and P.G.E.	2
	35

Table III

Indications	
Intractability	13
Suspicion of Malignancy	8
Massive hemorrhage	6
Obstruction	5
Recurrent Hemorrhage	3
	35

ter duodenostomy which entailed no particular difficulties in management. All patients were considered from the standpoint of nutrition and blood volume and defects corrected as much as possible preoperatively.

As can be seen from Table II, no attempt was made to present a series of one-type of surgical operation. Instead of this, the operative procedure was suited to the patient and the pathological changes encountered. If it was felt desirable to leave the antrum in place, the criteria established by Nyphus and Harkins were strictly adhered to;[4] that is, the antrum remained in the acid stream. It was subjected to complete gastric vagal denervation and antral stasis was prevented.

Subtotal gastrectomy was never carried higher than two-thirds because of the nutritional problems which are encountered postoperatively after high resections. If the patient had a particularly severe ulcer diathesis, a vagotomy was employed. This was done either in combination with a resection or with a drainage procedure. When a gastric resection was the procedure of choice, no decision was made as to the type of anastamosis until the resection was completed. At this time if a scarred, fixed duodenum remained, it was closed and a Bilroth II anastamosis performed. Otherwise a Bilroth I reconstruction was preferred.

All these cases were performed with constant gastric suction which was left in place for at least three days postoperatively. During this period of time vigorous therapy by the I.V. route was utilized to replace electrolyte loss and minimize protein anabolism.

Twenty-five patients had uncomplicated courses while the other ten presented fourteen separate complications. Urinary tract infection was encountered most frequently probably because of the use of indwelling catheters to measure urinary output accurately after long or stressful procedures. Pulmonary infection developed in two patients in spite of vigorous, supervised postoperative coughing regime. Prolonged paralytic ileus occurred in two patients. Single occurrences of other complications are listed in Table IV. All patients recovered. The patients were followed on the Ward at twelve hour intervals in the days that followed surgery. Early ambulation and leg exercises were prescribed and supervised. This may be in part responsible for the absence of thrombo-embolic complications. Feeding was started slowly after the third day and a good diet not reached until the 7th or 8th day. There were no cases of postoperative bleeding except one with nasal hemorrhage entailed from using an aspirator to remove mucoid secretions from the tracheobronchial tree in a patient with pulmonary infection. One re-operation was required for repair of a dehiscence.

Thirty-four patients were followed one to nine years. All of these patients reported being improved by their operation. The seven patients with mild dumping were, understandably, not as enthusiastic about the result as the other.[27]

It is interesting to compare the 26 resected with the 9 non-resected patients. Complications and dumping proved to be more common in the resected groups.

TABLE IV

Postoperative Complications	
Uncomplicated	25
Urinary tract infection	3
Pulmonary infection	2
Ileus	2
Obstruction	1
Infection	1
Dehiscence	1
Staphylococcal enterocolitis	1
Delerium Tremens	1
Pancreatic Fistula	1
Nasal Hemorrhage	1

TABLE V

Results	
Deaths	0
Markedly Improved	27
Moderately Improved	7
Unimproved	0
Lost to Follow-up	1

TABLE VI

Dumping Syndrome	
No Dumping	27
Mild Dumping	7
Lost to Follow-up	1

TABLE VII

Comparison of Resected and Non-resected Patients	*26 Resections*	*9 Vagotomy and Drainage*
Complicated	9	2
Dumping	6	1
Average post-op. stay	15 days	14 days
Markedly improved	20	7
Moderately improved	6	2

It is possible to conclude from this study that definitive gastric surgery can be of great value in the management of severe upper gastrointestinal pathology on the Community Hospital level. The procedure, carried out by those properly trained in them, can be performed with a low morbidity and mortality rate if the patient is carefully prepared for surgery and if the procedure is selected to meet the conditions encountered as far as the patient and his disease are concerned. It should always be borne in mind that surgery for peptic ulcer is not primarily the removal of a pathological organ but rather the alteration of an abnormal secretory state by a physiologically designed procedure.[5]

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Continued on Page 75

Mobilization and Examination of Respiratory Secretions for the Diagnosis and Treatment of Chest Diseases

BURTON M. COHEN, M.D., F.A.C.P.*

When bronchial catharsis is poor, and the amount and characteristics of respiratory secretions change, urgent and aggressive management must support the failing cough reflex, liquify the thick, tenacious sputum, unseat bronchiolar mucous plugs and open the airways. Sputum samples must be obtained in these, and other, situations as a "non-surgical biopsy" shedding light on the underlying specific bronchopulmonary pathology.

Deep-cough specimens, needed for accurate diagnosis, have been notable in revealing lung malignancies,[1-3] pneumonia[4] and fungus diseases.[5] In about 10% of all patients with pulmonary tuberculosis, induced-sputum samples are positive when conventional gastric aspirates are negative.[6,7]

Therapeutic sputum mobilization is needed in many medical and surgical situations. Acute respiratory tract infections, industrial and other pneumotoxins, atmospheric peculiarities[8] and coma are among the signal acute medical indications. Sputum evacuation is required in many neurologic disorders, chest wall diseases, diffuse pulmonary fibrotic and vascular pathology, mediastinal derangements, the lung complications of cystic fibrosis, in the alveolar hypoventilation syndromes, and where long-term inhalation therapy and mechanical aids to ventilation are carried out.[9] Bronchial cleansing is inefficient particularly in chronic obstructive ventilatory disease as cough reflexes become less helpful,[10] and the initially sterile mucoid sputum becomes purulent.[11] (Reid[12] has emphasized the primacy of irritation, acting alone, in leading to these changes, despite the contribution of secondary microbial action, and characterizes the hypertrophy of mucous-secreting airways structures as a final common pathway over which a host of irritants operate in chronic bronchitis, asthma and diffuse obstructive pulmonary emphysema.) (Table 1).

All surgery is marked by some impairment of lung function, during the induction phase, operation and the postoperative period, deviations of greater magnitude during heart and lung procedures and other operations of prolonged duration and increased complexity. The altered physiology results from hypoxia, alveolar underventilation, the combination of postoperative metabolic acidosis secondary to a falling cardiac output and respiratory acidosis associated with an increased physiologic dead space, from the increased work of breathing and the contributions of pre-existing medical disease, the use of analgesics, sedatives and tranquilizers,[13] and the development of atelectasis, pneumonia, pulmonary embolism and pneumothorax (Table 2).[14] The obese are particularly at risk. Additional "surgical" indications to encourage cough and remove secretions and foreign matter include injuries of the head, thorax and abdomen, as well as routine care of the patient with a tracheostomy.

TABLE I

SOME MEDICAL INDICATIONS FOR THERAPEUTIC SPUTUM MOBILIZATION*

I. *Acute Illnesses:*
- A. Bronchitis and Bronchiolitis
- B. Influenza
- C. The Pneumonias
- D. Atmospheric Factors
- E. Chemical Factors
  - 1. Industrial Pneumotoxins
  - 2. Smoke (Conflagration)
  - 3. Agricultural
- F. Coma
  - 1. Oxygen Lack
  - 2. Reduction in Nutrients
  - 3. Metabolic
    - a. Visceral Disease
    - b. Fluid-Electrolyte Derangements
    - c. Outside Influences:
      - 1) Temperature Variation
      - 2) Chemical Sources
        - a) Inorganic
        - b) Organic
        - c) Deficiency States
  - 4. Coma of Multiple Origin
    - a. Seizures, etc.
    - b. Increases in cerebrospinal fluid pressure
    - c. Brain Tumor
    - d. Head Injury
    - e. Infection
    - f. Syncope

II. *Chronic Illnesses:*
- A. Neurologic Disease
- B. Alveolar Hypoventilation
  - 1. With Obesity ("Pickwickian Syndrome")
  - 2. Primary, Idiopathic ("Ondine's Curse")
- C. Chest Wall Disease
- D. Mediastinal Disease
- E. Diffuse Pulmonary Vascular Disease
- F. Diffuse Pulmonary Fibrotic Disease
- G. Pulmonary Involvement in Cystic Fibrosis
- H. Bronchiectasis
- I. Prolonged Use of Therapeutic Gases and Mechanical Aids to Ventilation
- J. *THE OBSTRUCTIVE VENTILATORY DISEASES*

*Modified from Rosomoff, H.L., and Safar, P.[9]

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Read at the 1969 Annual Meeting, Maine Chapter, American Academy of General Practice, Portland, Maine, December 6, 1969.

TABLE 2

SOME SURGICAL INDICATIONS FOR THERAPEUTIC SPUTUM MOBILIZATION

I. During Anesthesia
II. During Surgery
III. In the Postoperative Period
  A. Hypoventilation Syndromes
  B. Atelectasis
  C. Pneumonia
  D. Pulmonary Embolism
  E. Pneumothorax-Hemothorax
  F. Pulmonary Complications of Cardiac Disease
IV. Routine Care of Tracheostomies
V. Post-Traumatic Disorders
  A. Chest-Abdominal Injuries
  B. Cranial Injuries

Let us consider first and separately techniques for producing bronchial samplings for diagnostic study, omitting assessment of the best methods of laboratory examination after the specimens are obtained.[15,16] Further, let us assume that we cannot obtain sputum from deep coughing with spontaneous expectoration. Bronchial washings, sometimes diagnostic, are of little value unless the lesion is bronchoscopically visible, and sputum samples, no matter how obtained, are more likely to yield positive findings, regardless of the visibility of the carcinoma.[17] Skill is crucial in delivering adequate washings and aspirates, a professional attribute varying widely.[18] Fortunately, a wide experience following Bickerman's initial demonstration of the value of inhalations of superheated aerosolized solutions of mixtures of saline and propylene glycol in facilitating expectoration[19] indicates that material satisfactory for cytologic study can be collected in as high as 99% of patients so-treated.[20–23] Using a modification of Bickerman's original method, we found that a superheated aerosol of 40 percent propylene glycol in isotonic saline** generated by an apparatus made from parts purchased at local appliance and drug stores for less than $12.00, provided adequate sputum samples for diagnosis in three-quarters to four-fifths of patients with little or no cough, after only one mist inhalation.[20] We now use an inextensive, superheated commercial apparatus nicknamed "the coffee pot" for obvious reasons. Abramowitz and Small[24] have shown that a saline-propylene glycol solution for this purpose can be given using a De Vilbis No. 42 nebulizer propelled either by an air tank at a 6-7 liter/minute flow, or by simply compressing the rubber bulb supplied with the nebulizer. Such simple equipment and the more elaborate office and hospital instruments should use disposable mouthpieces and basic parts easy to clean between patient sessions;[25] protection against cross-infection is afforded by safety hoods after the model developed by the Mayo Clinic workers.[26] If one suspects infection with Histoplasma Capsulatum, saline solutions should be used rather than propylene glycol mixtures because the latter may interfere with certain growth phases of the fungus.[5] Although our own experience in the diagnosis of tuberculosis with the mixtures is good, agreeing with the reports of others, at least one group has suggested that the simple saline solution may also be best in tuberculosis searches.[27]

Therapeutic mobilization of sputum rests upon the three principles of (1) dilatation of the airways, (2) liquefaction of retained matter and (3) evacuation of sputum and secretions (Table 3). Breathing exercises against graded resistance devices and through pursed lips is a fundamental maneuver which prevents airways collapse during exhalation and develops desirable changes in the bronchi, as a preface to other dilating modalities and a later concomitant of the latter.

Altered lung function in the patients who need our assistance results not only from the changed secretions, but from bronchospasm and swelling of the respiratory mucous membranes. So-called "bronchodilator" and "decongestant" drugs have been used to (1) relax smooth muscles in the tracheobronchial tree, and perhaps in the alveolar ducts and alveoli, (2) decongest and shrink the swollen mucous membranes, (3) aid lung clearance mechanisms by increasing ciliary motility and speeding mucous transport,[28] and (4) to prevent the adverse (bronchoconstrictor) effects which might be caused by other need modalities of therapy and drugs if the latter were given alone.

The xanthine derivatives and the sympathomimetic amines are the two categories of bronchodilator agents in general use. The xanthines are used orally, often combined with the sympathomimetic amines, and can be given intravenously or by rectal suppository; administration as an aerosol is little used, but reportedly helpful.[29] Although aminophylline compounds may produce undesirable gastrointestinal reactions, mixtures of this xanthine with antacids are acceptable and well-tolerated.[30]

Isoproterenol is the current prototype of the bronchodilator sympathomimetic amines, sharing with epinephrine its airways dilating effects but exhibiting less of the cardiovascular and nervous stimulating properties of the latter. When combined with phenylephrine, a strong decongestant and weak bronchodilator in its own right, the potency and duration of action of isoproterenol may be enhanced.[31–33] Isoetharine is another such compound with excellent bronchodilating properties by a variety of routes,[34] with an accompanying mild anti-hypertensive action that makes it desirable for use in patients with arterial hypertension and expiratory airflows disorders.[35]

For a variety of pharmacologic, physiologic and clinical reasons, aerosols are the popular and preferred method of giving sympathomimetic drugs. These may be given using a wide spectrum of systems, incorporating hand, motor and IPPB/I-driven nebulizers incor-

**The propylene glycol-saline mixture was prepared by dissolving nine 1-gram tablets of sodium chloride in 600 cc of distilled water and then adding 400 cc of propylene glycol, S.F. The mixture is shaken thoroughly before each use.[20]

TABLE 3

METHODS OF THERAPEUTIC MOBILIZATION OF SPUTUM AND SECRETIONS

I. *Dilate the Airways:*
- A. Breathing Exercises & Pursed-Lips Breathing
- B. Bronchodilator Drugs
  - 1. Oral
  - 2. Rectal
  - 3. Intravenous
  - 4. AEROSOL
    - a. Primary Bronchodilator Action
    - b. Aid in Mucous Transport
    - c. Forestall Deleterious Airways Effects of Other Therapy

II. *Liquefaction of Sputum and Secretions:*
- A. Increase Fluid Intake
- B. Humidification-Nebulization
  - 1. Warm Mists
  - 2. Nebulizer-Humidifiers with or without IPPB-I
    - a. Ultrasonic
  - 3. Solutions:
    - a. Water
    - b. Moistening, thinning and detergent agents
    - c. Enzymes and Mucolytics
- C. Specific Medications Used
  - 1. Bronchodilators of Isoproterenol Class
  - 2. Heparin
  - 3. Bland, moistening, thinning and detergent agents
    - a. Water
    - b. Saline
    - c. Propylene Glycol
    - d. Alevaire
    - e. Tergemist
  - 4. Specific Mucolytics:
    - a. Dornavac – for Purulent Secretions
    - b. Ascumist
    - c. MUCOMYST – for Mucoid Secretions

III. *Sputum Evacuation:*
- A. Forced Cough and Effective Cough Training
- B. Postural Drainage
- C. Percussion-Vibration
  - 1. Hand percussion
  - 2. Vibrators
  - 3. Vibrating Vest
  - 4. Cough Belts, etc.
- D. Superheated Aerosols
- E. IPPB-I
- F. EWNP (Cofflator)
- G. Bronchoscopy, Suction, Tracheostomy
- H. Combinations of A-G, inclusive.

porating heated, superheated, ultrasonic or pressure-assisted features, with and without oxygen sources. The most convenient method of administering these drugs is in the form of Freon®-generated, self-contained hand nebulizers which deliver a fixed amount of therapeutic agent with each depression of a metering valve. The virtues of this method have not escaped even the authors of popular spy novels.‡ Although there is much agitation at present about so-called "nebulizer deaths," sober reflection suggests that such mishaps may result not from use of the devices per se, but from reliance upon this method *alone* in situations requiring comprehensive laboratory evaluation and an aggressive program of management utilizing *many* aids from the host of different treatment resources available.[36]

Heparin® is another valuable agent which can relieve bronchospasm and aid in eliminating obstructing secretions,[37] although its direct broncholytic worth is less than that of isoproterenol.[38]

After dilatation of the conducting passages, liquefaction and sputum expulsion are less difficult. Adequate body water is critical in sputum mobilization, so that water is considered "a major therapeutic agent . . . and the most important of all aerosols."[39] In a patient able to take liquids, tripling the fluid intake by mouth may cut sputum viscosity by two-thirds.[40] Normal humidification of inspired air in the nasal passages and pharynx may then be sufficient. However, humidification is frequently impaired. This may occur when a medically ill, injured or postoperative patient becomes dehydrated through various degrees of high water needs, excess water loss and low water intake in differing individual combinations. Normal humidification is inadequate or bypassed when there is a tracheostomy or an endotracheal tube is in place. Allergy, injury, infection may all attack the nasopharyngeal lining and compromise humidification. Therapeutic gases which are dry also call upon this weakened mucous membrane to alter the vapor-free inspired load. Finally, a dry, crusted coating of secretions forms, sometimes tolerated without overt distress for a brief time by adults, but the cause of airway obstruction in the smaller passages of infants and small children.

Egan suggests that much confusion concerning water inhalation is avoided if we use the term *"vapor"* to refer to water vapor in its gaseous or "molecular," invisible form, and "aerosol" to include mist, cold steam and fog, that is, water in fine particulate form, visible on light diffraction.[39] We give the amount of water vapor in a given volume of gas in terms of absolute and relative humidity. In respiratory therapy, the term "percent body humidity" is used, alluding to the amount of water vapor in a volume of gas as the percent of the water in gas saturated at body temperature.

The water content of a saturated gas depends upon its temperature; if gas, saturated with water vapor at 0° C is heated to 37° C, the water content must be increased from 5 to 44 mm Hg. per liter to keep saturation.[41] Particle size is also important in treatment, most particles over 4 micra in size settling in the upper airway, under 50% 1 micra in size depositing in the alveoli.[42] Breathing rates are also relevant, with less deposition at faster rates of respiration.[43]

Ordinary bubble humidifiers and unheated nebulizers are used to moisten dry oxygen and gas mixtures, but reduced temperatures are common in their reservoirs,

‡"Modern physicians used a device for spraying various drugs in powder form into the bronchi. Medihalers® or snuff gave a more rapid absorption into the blood stream where certain chemicals were concerned than when swallowed in pill form. Medihaler powder could produce results which were almost instantaneous." – George B. Mair, THE GIRL FROM PEKING, Berkley Publishing Corporation. 1967, New York.

so that these methods provide adequate humidification only for facial mask and nasal catheter methods.[44] Humidification is enhanced by heating the water to be aerosolized, so that the temperature drop taking place during transit to the patient is overcome. The tubing used should be sufficiently large, and the distance travelled as short as possible so that water condensation with these heated units does not block the flow of gas or waste the high liquid content.[44] Humidification is also improved if the gas in the humidifier is supersaturated with water particles of relatively uniform, and small, size, using a water reservoir system in which the compressed gas is directed through a Venturi opening, or by means of a spinning disk nebulizer.

Superheated nebulizers are as important here as they are for induction of sputum for diagnostic purposes; if we give hypertonic salt solutions by this means water is drawn into the bronchial lumen, loosening the secretions and preparing them for expulsion. Although 10-20% propylene glycol solutions may retard droplet evaporation, stabilize particle size and increase the amount of water available for deposition deep within the lungs,[45] this is still controversial.[46] Clinically, propylene glycol solutions, often containing isoproterenol with and without phenylephrine, are well tolerated and useful,[47] particularly when pressure-assisted methods of delivery may not be desirable.

The ultrasonic nebulizer is enjoying wide use today.[48] The power unit of these devices changes ordinary alternating house current to ultra-high frequency energy which is transmitted to a piezoelectric transducer in the shape of a small ceramic cupped disc in the nebulizer element. When this disc, which holds a small amount of water, vibrates sympathetically to the energy applied to it, so does the enclosed water, and the water in the larger, nebulizer, compartment in which the disc is seated. The transmitted vibrations break up the water in the nebulizer into a large volume of small particulate size; heating is not needed, and up to 6 cc of water can be nebulized per minute, a rate of delivery which is independent of the flow rates of the gases employed. Ultrasonic nebulization is of major value in achieving maximum liquefaction by dilution of tracheobronchial secretions, as well as maximum humidification of the inspired air; cough can be stimulated for therapeutic and diagnostic reasons. The signal indication for ultrasonically produced aerosols is in pediatric diseases accompanied by obstructing secretions, chiefly cystic fibrosis with bronchopulmonary involvement, and croup. The efficiency of the aerosol produced is so great that care is necessary to prevent overhydration of the infant or child. This requires frequent weighing and subtraction of the weight rise from the humidified air from the total water needs. It is also felt by some that sterile water, rather than saline, should be used because the pediatric patient's immature kidneys may not handle the salt load adequately.[49]

We must know more about the possible hazards of long-term use of ultrasonic nebulization. Lesions resembling bronchopneumonia have been produced in animals exposed to ultrasonically-generated mists for long periods.[50] Unlike solutions given by heat nebulizers, those nebulized by ultrasound have been shown to increase airway resistance, an undesirable action for individuals with expiratory airflow disorders; sympathomimetic bronchodilator amines should be given immediately prior to use of ultrasonic inhalation to forestall the bronchoconstrictor influences of the latter.[51] Lastly, it is imperative that all solutions used to sterile to prevent bacterial multiplication and continuous supply of infected material.

In addition to the bronchodilator amines and related decongestants, bland, moistening, thinning, detergent and mucolytic agents are used to liquefy the sputum and make it available for cough and expectoration. Dilute aqueous solutions such as 2.5% propylene glycol or 1.0% saline are examples of the bland solutions. Solutions based upon tyloxapol and sodium ethasulfate (commercially available as Alevaire® and Tergemist,® respectively) are the most frequently used wetting or "detergent" agents. Reviewing the clinical and laboratory data concerned, Egan concludes that these do have a limited effect on bronchial secretions which they render less viscid to supplement the efforts of cough, and are effective in increasing the contact of other active substances with the respiratory mucous membranes.[39] In a recent study[52] we found that large volume tyloxapol aerosols exhibited statistically superior effects over water inhalation in improving airway resistance, specific airway resistance, maximal mid-expiratory flow rate and air trapping indices, response differences we considered due to the better mobilization of retained secretions and bronchial catharsis following the former.

Aggressive management of obstructing secretions requires the use of "mucolytic agents." One of these, deoxyribonuclease (Dornavac®) is, actually, of little value against purely mucoid secretions, but is highly effective in the treatment of purulent secretions which are largely composed of DNA which it depolymerizes. Clinically this would be needed in acute tracheobronchial infections, pneumonia, bronchiectasis, lung abscess, and cystic fibrosis. Dornavac is given as 100,000 units three times daily as a small-particle aerosol, or may be instilled through the bronchoscope, if need be. It may be degraded by some metals and solutions used in inhalation therapy and is best given in clean plastic or glass nebulizers after fresh preparation for each treatment.

There are two mucolytic agents worthy of mention. One, oxymix, (Ascumist®) is an experimental preparation containing ascorbic acid, copper sulfate and sodium perborate which has been well-tolerated in clinical trials where its used was accompanied by betterment of breathing measurements, increased sputum volume and a decrease in sputum "apparent" viscosity.[53]

N-acetyl-L-cysteine (Mucomyst®) is a clinically available mucolytic with a specific activity for mucoproteins

and a less direct action on DNA and hyaluronic acid.[54] Truly mucolytic, its decreases the viscosity of mucoid sputum in direct proportion to its concentration, and numerous papers support its effectiveness in acute and chronic bronchopulmonary diseases, during anesthesia and surgery, in the postoperative period, for the post-traumatic chest, tracheostomy care, the lung involvement of cystic fibrosis and in the treatment of atelectasis secondary to mucous obstruction. In a controlled comparison, Kory and associates[55] found that nebulized acetylcysteine combined with racemic epinephrine was highly successful in thinning the sputum of patients with chronic obstructive bronchitis, while nebulized saline plus bronchodilator tended to make the sputum of the same individuals thicker. Bronchial obstruction previously seen with the mucolytic alone by these observers[56] did not occur when it was nebulized with racemic epinephrine. We agree that whenever acetylcysteine is given, as with most of the therapies outlined, a bronchodilator should be given before or concomitantly with this agent.

Acetylcysteine reacts chemically with rubber, iron, copper and other substances which are often components of inhalational equipment. Any portion of apparatus which may come in contact with the enzyme should be made of glass, plastic, aluminum, chromed metal, silver, tantalum or stainless steel. Side effects, usually minimal, consist most frequently of nausea or nasopharyngeal burning sensations.

The package insert for this agent, and a comprehensive publication by the manufacturer[57] contain comprehensive details of dose and method of preparation for instillation of acetylcysteine through the bronchoscope of catheter, into a tracheostomy or endotracheal tube, and as an aerosol delivered from nebulizers connected with face masks and tents, enclosing or partial oxygen tents, via mouthpieces or with attachment to IPPB/I apparatus for mechanical ventilatory assistance. The producers of acetylcysteine have developed a compact, durable, and inexpensive nebulizer-compressor system appropriate for delivering aerosols of this drug and other medications at home, in the clinic, hospital or physician's office. We have found this (Maxi-Myst Aerosol Unit®) device helpful not only for office treatments, per se, but for patient instruction preparatory to prescription of the apparatus for home use.

During dornase and acetylcysteine therapy, an increased volume of rapidly liquefied bronchial secretions may occur which may not be expectorated if the cough reflex is weak, faulty or absent. The physician or his delegate therapist must stand ready to maintain a patent airway with suction, endotracheal aspiration or bronchoscopic assistance.

Effective coughing is critical to the success of the foregoing two steps of sputum mobilization and requires active encouragement in most patients. Where pain, fear, abdominal and thoracic bindings and dressings or a cast restrict respiration, the therapist supports the lower thorax manually and compresses the chest forcibly at the beginning of exhalation. The patient with obstructive ventilatory disease where air trapping is common, or the patient weaned from mechanical aids to respiration is taught to handle smaller volumes of air with each cough, beginning his exhalation from the mid- rather than the full-inspiratory position and is supported in exhalation in short, acute bursts of coughing rather than in a single, tiring cough.[39,58] Assistance in chest physical therapy is given by antecedent use of an aerosol bronchodilator, staged postural drainage and active chest manipulation. Direct percussion with sharp blows of the cupped hands applied alternately over the area of greatest involvement may be combined with postural drainage maneuvers. Vibration by application of the hands, or use of masseuse' or barber's hand vibrator is a useful, gentler method of moving secretions. Barach has summarized concisely the methods of manual and assistive mechanical thoraco-abdominal compression.[59] Beck has treated patients whose airways disease was complicated by secretions or structural changes with an ingenious vibrating thoraco-abdominal compression vest which improved respiration and expectoration by producing an expiratory pressure of 30 mm Hg. interrupted by vibrations at 1,800 cycles per second.[60]

All of the foregoing can be reinforced or incorporated in sessions utilizing one of a variety of IPPB-I machines designed to dilate the air passages, equalize distribution of inspired air and traverse areas of obstruction. Maximal benefits in supporting cough, supplying aerosolized medications, reducing the work of respiration, improving altered oxygen/carbon dioxide patterns and correcting respiratory flow patterns are obtained only by careful patient indoctrination by trained therapists acting-under the supervision of knowledgeable physicians.[61] When tenacious mucous plugs obstruct the airway, the use of helium-oxygen mixtures to traverse the narrowed passages may be more helpful than standard nitrogen-oxygen administration. The indications and hazards of such mechanical assistance should be reviewed before IPPB-I is instituted.[39,61]

Extensive study by Barach and associates led to the development of yet another means of mechanically supporting cough- EWNP (exsufflation with negative pressure).[62] The EWNP device ("Cofflator") consists of a high speed blower motor unit which introduces into the lungs via a patient mask or mouthpiece, a large air volume. At the moment of peak inspiratory pressure, which can be pre-set at a range from 20 to 40 mm Hg., a valve is automatically switched to a similar negative pressure, producing a sharp pressure drop which sweeps secretions and foreign matter mouthward. The length of inspiration and expiration can be regulated. The rapid fall in pressure within 0.02 second's time produces an expiratory flow-rate equal to, or surpassing that of natural, normal, vigorous cough, effects not generally attained after IPPB-I sessions. Like the latter, EWNP treatments may enhance diaphragmatic motion, im-

prove ventilation and drainage of the lungs, and induce favorable changes in abnormal blood gas patterns and pH deviations. Proper application again requires knowledge of the apparatus, the techniques of correct patient instruction and supervision, and awareness of requisite precautions and potential hazards.[61]

Once learned, most of these modalities will be put to use by the family physician in a variety of individually-tailored treatment programs and diagnostic areas frequently required in his daily practice for patients from infancy to old age. As Wigglesworth observed, nearly three centuries ago:

"New-England, where for many years
You scarcely heard a cough,
And where Physicians had no work,
Now finds them work enough."[63]

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Allowable Benefits — Medicare, Part B

The charge patterns determining usual, customary, and prevailing fees are well established. The Carriers are now required to devote more of their administrative efforts to utilization review. Medicare regulations state: "No payment may be made under Medicare for any expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

When numerous injections or repetitive diagnostic tests are medically necessary, some explanatory notation should accompany the claim. Utilization refers to frequency and need of office, home, nursing home and hospital visits, frequency and need of laboratory, x-ray, and other diagnostic studies, frequency and need of injections and other treatments such as physical medicine modalities.

The subject of utilization as it effects the cost of medical care has attracted the attention of the American Medical Association, Congress, Department of Health and Welfare, Social Security Administration, labor, the public and the press. Special attention to these factors by all physicians would minimize questionable correspondence referable to the complete necessity of all items listed. — **From Medicare Health Insurance Part B, Box 4629, Portland, Maine.**

X-Ray Of The Month*

This newborn infant girl experienced respiratory distress at birth. Nasal suction catheters could not be passed. The clinical diagnosis was confirmed radiographically.

Bilateral Choanal Atresia

This recent MMC case reemphasized the fact that this particular anomaly represents a surgical emergency in the newborn.[1] It has been suggested that this entity may well be responsible for some cases of unexplained neonatal asphyxia.[3] The mechanism of respiratory obstruction is not clear in the infant with bilateral choanal obstruction. It has been suggested that the tongue is sucked up against the palate on inspiration and then in expiration the soft palate is ballooned forward against the tongue. Whatever the mechanism, some of these infants seem unable to mouth-breathe, while others adapt quickly. Those infants not adapting require constant nursing attention until proper corrective surgery can be instituted.

Embryologically, the most likely mechanism is persistence of the nasobuccal membrane which usually ruptures in the seventh week of fetal life.[2]

The radiologic confirmation of this clinically suspected diagnosis is simple. A lateral projection (with the central ray parallel to the floor) of the skull with the patient supine, is obtained after nasal instillation of an iodized oil. As in the case presented, the pooling of this contrast material in the posterior nasal cavity confirms the diagnosis. A Hirtz projection is recommended to show the bilateral nature of the anomaly.

*From the Department of Radiology, Maine Medical Center, Portland, Maine 04102.

References

1. Cohen, H. J. and Witchell, J. S.: Bilateral Congenital Choanal Atresia in Newborn. Am. J. Dis. Child. 83: 328-332, 1952.
2. Peer, L. A.: Congenital Anomalies of the Nose and Sinuses. Otolaryngology, Vol. 3, Chap. 4: W. F. Prior Co., Inc., Hagerstown, Md., 1955.
3. Morrow, R. C.: Bilateral Choanal Atresia, A Surgical Emergency in the Newborn. Journal of the Maine Med. Assoc. 49: 135-136, 1958.

PROTEIN CONTENT / 7 oz. Serving*

Bean with Bacon	6.8	Green Pea with Ham (Frozen)	7.6
Beef	8.0	Hot Dog Bean	8.4
Chicken Broth	5.5	Pepper Pot	6.1
Chicken 'N Dumplings	5.8	Split Pea with Ham	10.2
Chili Beef	6.2	Vegetable Beef	5.0
Green Pea	6.9	Vegetable with Beef (Frozen)	5.4

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* From "Nutritive Composition of Campbell's Products" which gives values of important nutritive constituents of all Campbell's Products. For your copy, write to Campbell Soup Company, Dept. 365, Camden, New Jersey 08101.

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The efficiency of Pro-Banthine—its favorable balance of therapeutic and secondary actions—has been thoroughly tested and observed. This quality has been demonstrated surgically, roentgenographically, cinegastroscopically and, above all, clinically.

When physicians needed to relax the restless duodenum for the recently refined technic of hypotonic duodenography they logically turned to Pro-Banthine.

For years Pro-Banthine has been the most widely used anticholinergic medication for calming the gastrointestinal tract—for suppressing secretion, prolonging the action of antacids and providing the proper environment for healing peptic ulcers.

These established therapeutic actions make Pro-Banthine particularly useful in:

- peptic ulcer
- gastritis
- diverticulitis
- irritable colon
- biliary dyskinesia
- functional hypermotility

We wish to thank Drs. Marcia K. Bilbao, Louis H. Frische, Josef Rösch and Charles T. Dotter for this exceptionally graphic example of hypotonic duodenography.

Contraindications: Glaucoma, severe cardiac disease.

Precautions: Since varying degrees of urinary hesitancy may occur in elderly men with prostatic hypertrophy, this should be watched for in such patients until they have gained some experience with the drug. Although never reported, theoretically a curare-like action may occur with possible loss of voluntary muscle control. Such patients should receive prompt and continuing artificial respiration until the drug effect has been exhausted.

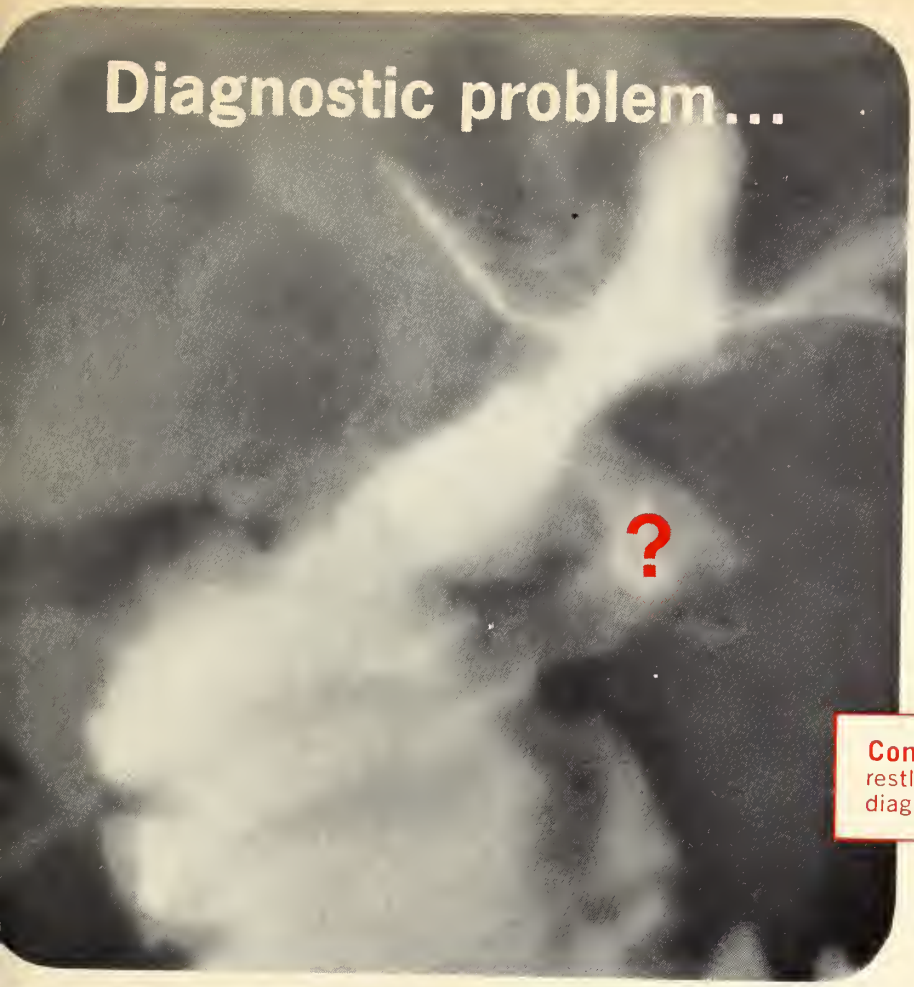
Side Effects: The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.

Dosage: The maximal dosage tolerated without excessive side effects is usually the most effective. For most adult patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two 15-mg. tablets four to six times daily may be required. Pro-Banthine (brand of propantheline bromide) is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg. The parenteral dose should be adjusted to the patient's requirement and may be up to 30 mg. or more every six hours, intramuscularly or intravenously.

982

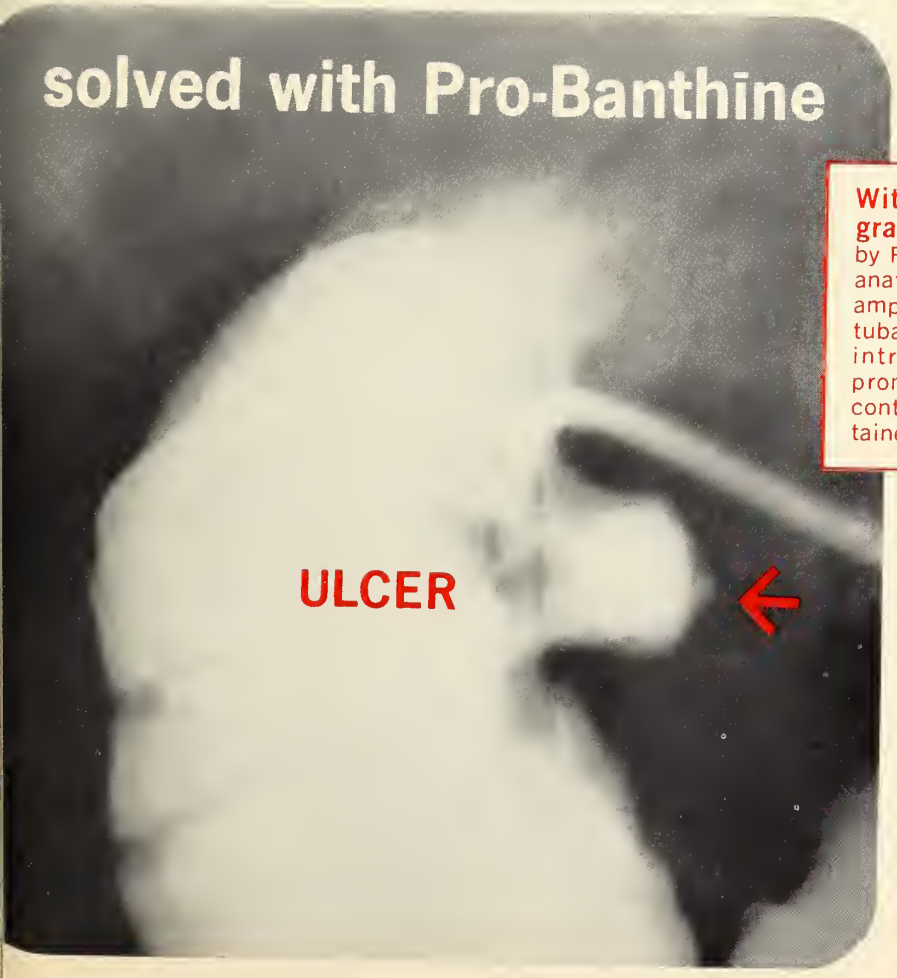
SEARLE *Research in the Service of Medicine*

Diagnostic problem...



Conventional x-rays of the restless duodenum are often diagnostically indefinite.

solved with Pro-Banthine



With hypotonic duodenography duodenal calm induced by Pro-Banthine permits clear anatomic appraisal. In this example the duodenum was intubated. Pro-Banthine, 60 mg. intramuscularly, produced prompt aperistalsis. Double contrast visualization was obtained with barium and air.

Nose clear as a whistle

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Dimetapp Extentabs® does an outstanding job of helping to clear up the stuffiness, drip and congestion of colds and upper respiratory allergies and infections. Each Extentab keeps working up to 12 hours. And for most patients drowsiness or overstimulation is unlikely. Try Dimetapp. It clearly works.

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UP TO 12 HOURS CLEAR BREATHING ON ONE TABLET

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Contraindications: Hypersensitivity to antihistamines. Not recommended for use during pregnancy.
Precautions: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension.
Side Effects: Hypersensitivity reactions including skin rashes, urticaria, hypotension and thrombocytopenia, have been reported on rare occasions. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered.
Dosage: 1 Extentab morning and evening.
Supplied: Bottles of 100 and 500.

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117th Annual Session of the Maine Medical Association

The Colony, Kennebunkport, Maine June 7, 8, 9, 1970

The annual meeting of the Maine Medical Association this year will offer to you and to one of your office personnel, if you wish, an opportunity to gain, at firsthand, knowledge of some of the newer modes of acquiring and recording medical information — the automated medical history. We urge you to be an active participant in this program.

This section of the program has two parts:

1) The automated health questionnaire

2) The physical examination

It will be possible to process several hundred automated health questionnaires during the meeting, but time and personnel will permit only 100 physical examinations (including pulmonary function tests, vision and hearing tests, electrocardiogram, stool guaiac, laryngoscopy, proctoscopy and laboratory studies). All of this data will be available to the participant and to his personal physician. There will be an opportunity, in most instances, to have these findings reviewed and a problem list outlined by a physician familiar with a systematic approach to health care.

HAROLD D. CROSS, M.D., Hampden Highlands, Maine
Chairman, Scientific Committee

Guest Speakers For This Program Include . . .

- Warner V. Slack, M.D. of Madison, Wisconsin — "Medical History Taking, Automated Techniques, Reliability"
- John C. Bjorn, M.D. of Hampden Highlands, Maine — "Allied Health Personnel, Their Use in Physiological Testing, Screening Procedures"
- Charles S. Burger, M.D. of Washington, D.C. — "Use of Allied Health Personnel in the Military — AMOS Program"
- Lawrence Weed, M.D. of Burlington, Vermont — "Is the Computer Really Going to Help the Doctor?"
- Charles S. Burger, M.D., John C. Bjorn, M.D., Lawrence Weed, M.D. and Harold D. Cross, M.D. — (Workshops — 4 Groups) — "Formulation of Problem List, Plans and Follow-up"
- Bradley E. Brownlow, M.D. of Blue Hill, Maine, Lawrence Weed, M.D., Charles S. Burger, M.D., John C. Bjorn, M.D. and Warner V. Slack, M.D. — Panel Discussion: "Questions and Answers Regarding Problem-Oriented Medical Record, Computers, Allied Health Personnel, Automated Techniques"

Other Featured Speakers Include . . .

- Thomas A. Martin, M.D. of Portland, Maine — Moderator of Panel Discussion: "The Closed Reduction of Common Fractures and Their Pitfalls"
- Carl S. Blyth, Ph.D. of Chapel Hill, North Carolina — "North Carolina High School Football Injury Study"
- Philip Kramer, M.D. of Boston, Massachusetts — "Medical Aspects of Ulcerative Colitis"
- Lester F. Williams, M.D. of Boston, Massachusetts — "Surgical Aspects of Ulcerative Colitis"

Specialty Group Meetings . . .

- Maine Chapter of the American Academy of Pediatrics
- Section on Ophthalmology of the M.M.A.
- Maine Society of Clinical Hypnosis
- Maine Society of Internal Medicine
- Maine Psychiatric Association
- Maine Radiological Society
- Ear, Nose and Throat Group

Watch Your Mail For . . .

Program Details . . .

Specialty Group Programs . . .

Reservation Forms . . .

Woman's Auxiliary To The M.M.A.

The Woman's Auxiliary to the Maine Medical Association will be holding their annual meeting in conjunction with the 1970 annual session of the Maine Medical Association on June 8th, with York County acting as hostess. The program for their group will be included in the M.M.A. program.

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Statement On Criteria For Evaluation Of Long-Acting Coronary Vasodilators In Treatment Of Angina Pectoris

The evaluation of an agent claimed to be effective in the management of angina pectoris in other than an acute attack should be based on convincing evidence that long-term administration of the agent does prevent or decrease the incidence and/or the severity of anginal pain. Unfortunately, meaningful objective evidence is difficult to obtain. . . .

The problems inherent in designing a meaningful study are numerous. . . . :

(1) In most patients there is a spontaneous fluctuation in the frequency and severity of angina pectoris. . . .

(2) . . . . seasonal factors should be considered in planning a drug evaluation.

(3) The patient with angina pectoris is responsive to reassurance. . . . The placebo effect may be such that 50% or more of the patients will claim to have been benefited.

(4) Some patients respond well to nitroglycerin, others moderately, and still others not at all. This must be borne in mind when the number of tablets . . . that are taken daily by a patient is used as a measure of angina. . . . Because the physician must depend on the word of the patient in characterizing the severity or duration of anginal pain, his estimate of patient reliability . . . is important.

(5) The electrocardiographic exercise test has been proposed as an objective measure of patient response to anti-anginal drugs. Although the exercise test may provide objective data, results are not conclusive. . . . Thus, this test can indicate only the anticipated, but not the actual, benefit of the test drug.

In view of these considerations, and despite the difficulties of clinical evaluation, a clinical approach must be used. After an extensive review of the literature, it is evident that no study has been reported that has taken into consideration all of the variables inherent in observing anginal pain. The one study that most closely fulfills the criteria outlined above led to the conclusion that the long-acting nitrates tested were without benefit. . . .

In summary, the Panel concludes that the efficacy of long-acting coronary vasodilators has not yet been adequately established. . . .

Submitted by Jacob B. Dana, M.D., Maine Heart Association

Reference: Report of the Panels on Cardiovascular Drugs from the Drug Efficacy Study: Circulation, Vol. XLI, pages 149-151, 1970

Necrologies

George R. Landwehr, M.D.

1923-1969

George R. Landwehr, M.D., 45, of Augusta, Maine died on November 15, 1969. He was born in New York City on December 19, 1923, son of George A. and Nellie Ellen Landwehr.

Dr. Landwehr was graduated from Columbia University in 1945 and received his medical degree from New York University School of Medicine in 1947. He interned at the French Hospital in New York City from 1947 to 1949. From 1950 to 1956, Dr. Landwehr practiced medicine in Cincinnatus, New York. He served in the Navy as Lt. Commander from 1956 to 1958 and then served three years residency in obstetrics and gynecology at the Ellis Hospital in Schenectady, New York. In 1961, Dr. Landwehr moved to Augusta where he went into practice in obstetrics and gynecology.

He was a member of the Kennebec County Medical Association, the Maine Medical Association, the American Medical Association, the American College of Obstetrics and Gynecology and was a diplomate of the American Board of Obstetrics and Gynecology.

Surviving are his widow, Anastasia McLean Landwehr; a son, Roderick; two daughters, Patricia and Gretchen Landwehr, all of Augusta; and his father, of Lakewood, New Jersey.

Albert M. Carde, M.D.

1896-1969

Albert M. Carde, M.D., 73, of Milo, Maine died on November 30, 1969. He was born in Bowdoinham, Maine on September 20, 1896, son of Joel and Marie Houdlette Carde.

Dr. Carde was graduated from Hebron Academy, attended the University of Maine and received his medical degree from Bowdoin Medical School in 1919. He had taken postgraduate courses at various Boston hospitals in conjunction with Harvard and Tufts Medical Schools and the University of Buffalo, New York. Dr. Carde interned at the Maine General Hospital in Portland, Maine and started his practice in Lakeview in 1920 and moved to Milo in 1925.

He was an honorary member of the Piscataquis County Medical Society and the Maine Medical Association, having received a fifty-year pin at the June 1969 annual session. Dr. Carde was also a member of the American Medical Association, the American College of General Practitioners, was the Piscataquis County medical examiner many years and was the surgeon for the American Thread Company at Milo.

Surviving are his widow, the former Laurel Moores; a son, Philip R. of Augusta; a daughter, Miss Marilyn Carde of Milo; a brother, Ernest Carde of Gardiner; and three grandchildren.

Wesley C. McNamara, M.D.

1895-1970

Wesley C. McNamara, M.D., 74, of Lincoln, Maine died on January 13, 1970. He was born in Youngs Cove, New Brunswick, Canada on May 17, 1895, son of John and Tamar McNamara.

Dr. McNamara was graduated from Mount Allison College in Sackville, New Brunswick. He worked as a teacher for several years and in 1927 received his medical degree from McGill University Faculty of Medicine in Montreal.

Dr. McNamara took postgraduate courses at Western Branch, Montreal General Hospital and Jefferson Hale Hospital in Quebec and in 1928 opened an office in Brownville Junction. In 1929, he moved to Lincoln and maintained an office there for thirty-five years.

He was a member of the Maine Medical Association and the American Medical Association, a past president of the Penobscot County Medical Association, a former Penobscot County medical examiner, a former member of the Eastern Maine General Hospital staff and company physician for the Eastern Corp. in Lincoln for many years. Dr. McNamara was also a member of the Lincoln Masonic Lodge, and had served in the Canadian Army during World War I.

Surviving are his widow, Mrs. Ruth Peabody McNamara of Lincoln; a brother, Lester of Youngs Cove Road, New Brunswick; and several nieces and nephews.

Richard L. Savage, M.D.

1899-1969

Richard L. Savage, M.D., 70, of Fort Kent, Maine died on December 26, 1969. He was born in Fort Kent, Maine on January 1, 1899, son of William and Edith Daigle Savage.

Dr. Savage was graduated from Montreal College and received his medical degree from the University of Montreal Faculty of Medicine in Montreal in 1925. He took postgraduate courses at Notre Dame in Montreal and Clair's in New Brunswick. In 1926, Dr. Savage started his practice in Fort Kent.

Dr. Savage was a member of the Aroostook County Medical Society, the Maine Medical Association and the American Medical Association. He was also medical examiner for ten years and health officer for several years.

Surviving are his widow, Mrs. Germaine Picard Savage; a son, Carl of Fort Kent; a daughter, Mrs. William Young of Redlands, California; a sister, Mrs. Patrick Ryan of Littleton, New Hampshire; and four grandchildren.

County Society Notes

PENOBSCOT

The Penobscot County Medical Society met on December 16, 1969 with the President, Lloyd Brown, M.D., presiding.

Hans A. Holzwarth, M.D. introduced the guest speaker, Bruce Bower, M.D., Endocrinologist at Hartford Hospital. Dr. Bower's subject was Phosphate Therapy. He covered stones, bones and hypercalcemia. Bone was described as being kinetic like other tissues. Phosphate therapy never fails to lower serum calcium, enhances bone formation, healing of fractures and is effective in treatment of osteoporosis. Dr. Bower stated that certain individuals produce urine which is unstable tending to produce stones. Administration of phosphate stabilizes the urine. Pyrophosphate and short peptide chains are thought to be effective in stabilizing the urine.

George W. Wood, III, M.D. reminded the group of a warning notice on certain catheter trays produced by C. R. Bard. They are being recalled because of the presence of pseudomonas in the package. He also spoke of the concern of the AMA with health care particularly of the poor and new approaches to this problem will be forthcoming.

Robert O. Kellogg, M.D. remarked that health care of the poor is being explored by local groups and support of the Society is invited. Robert P. Andrews, M.D. moved that the Society support the program as outlined by Dr. Kellogg and that an Ad Hoc Committee, including Dr. Kellogg, be appointed. This was voted.

The annual election was then held with a slate of officers proposed by the nominating committee: Drs. Herbert C. Gilman, William A. Purinton and Leonard G. Miragliuolo. This was voted in as follows:

President, Edward L. Curran, M.D., Bangor
President-elect, Charles D. McEvoy, Jr., M.D., Bangor
Secretary, Lewis E. Phillips, M.D., Bangor
Treasurer, Ronald R. Striar, M.D., Bangor
Councilors, Drs. Benjamin L. Shapero, Bangor (3 yrs.), John S. Houlihan, Bangor (2 yrs.) and Russell M. Lane, Orono (1 yr.)
Delegates to the M.M.A. House of Delegates, Drs. Leonard G. Miragliuolo, Thornton W. Merriam, Jr. and Stanley J. Evans, all of Bangor, John J. Pearson, Old Town and Herbert C. Gilman, Millinocket. Alternates, Drs. George O. Chase, John F. McGinn and J. Robert Feeley, all of Bangor, Wilfred I. Butterfield, Lincoln and Russell M. Lane, Orono

Lloyd Brown, M.D. expressed appreciation for cooperation during the past year, but noted that the time of elections and tenure of the President is restrictive.

The meeting was then turned over to Dr. Curran, and with no further business, was adjourned.

WILLIAM M. SHUBERT, M.D., *Secretary*

YORK

The annual meeting of the York County Medical Society was held at the Goodall Hospital in Sanford, Maine on January 14, 1970.

Following the social hour and dinner, the business meeting was held.

Guest speakers included O. Thomas Feagin, M.D., Acting Director of the Communicable Disease Division of the Department of Health and Welfare, who gave a resumé of the German Measles Vaccine Program in the State. The featured speaker of the meeting was Jacob B. Dana, M.D., Togus, Maine. He discussed certain aspects of Coronary Heart Disease. He is Chief of Cardiology at the Veterans Administration Center, Togus, Maine and President of the Maine Heart Association.

The nominating committee composed of Drs. Kenneth E. Leigh, Chairman, James S. Johnston and Irvin Dorfman sub-

COUNTY SOCIETY OFFICERS

ANDROSCOGGIN

President, Lionel R. Tardif, M.D., Lewiston
Secretary, Donald L. Anderson, M.D., Lewiston

AROOSTOOK

President, I. Mead Hayward, M.D., Caribou
Secretary, George J. Harrison, M.D., Houlton

CUMBERLAND

President, George F. Sager, M.D., Portland
Secretary, Douglas R. Hill, M.D., South Portland

FRANKLIN

President, Wallace H. Duffy, M.D., Farmington
Secretary, Hays G. Bowne, M.D., Farmington

HANCOCK

President, Randall H. Silver, M.D., Ellsworth
Secretary, Bradley E. Brownlow, M.D., Blue Hill

KENNEBEC

President, George I. Gould, M.D., Richmond
Secretary, Francis A. Spellman, M.D., Togus

KNOX

President, Johan Brouwer, M.D., Rockland
Secretary, Alan F. Woodruff, M.D., Rockland

LINCOLN-SAGADAHOC

President, Arkadij Oceretko, M.D., Bath
Secretary, George W. Bostwick, M.D., Newcastle

OXFORD

President, Warren C. Hazelton, M.D., South Paris
Secretary, Hagop Halladjian, M.D., Rumford

PENOBSCOT

President, Edward L. Curran, M.D., Bangor
Secretary, Lewis E. Phillips, M.D., Bangor

PISCATAQUIS

President, John B. Curtis, M.D., Milo
Secretary, Isaac Nelson, M.D., Greenville

SOMERSET

President, Carlton E. Swett, M.D., Skowhegan
Secretary, John P. Dow, M.D., Pittsfield

WALDO

President, Norman E. Cobb, M.D., Belfast
Secretary, Euclid M. Hanbury, M.D., Belfast

WASHINGTON

President, George B. Shaw, M.D., Machias
Secretary, Karl V. Larson, M.D., East Machias

YORK

President, Maurice Ross, M.D., Saco
Secretary, Charles W. Kinghorn, M.D., Kittery
Asst. Secretary, Melvin Bacon, M.D., Sanford

mitted the following slate of officers who were unanimously elected:

President, Maurice Ross, M.D., Saco
Vice-President, Joseph M. Laltoo, M.D., York
Co-Secretary-Treasurer, Charles W. Kinghorn, M.D., Kittery and Melvin Bacon, M.D., Sanford
Delegates to the M.M.A. House of Delegates, Drs. Carl E. Richards, Sanford, Thomas Anton and Leopold A. Viger, both of Biddeford. Alternates, Drs. Kenneth E. Leigh, York, Marion K. Moulton, West Newfield and Irvin Dorfman, Biddeford

Robert F. Ficker, M.D., Kennebunkport, Councilor to the Maine Medical Association for York and Cumberland Counties, spoke on matters relative to the Council of the Maine Medical Association. He discussed the workings of the Council in brief and urged all members of the Society to read the articles in the December 1969 issue of The Journal of the Maine Medical Association entitled "Understanding What's Important" and "What's Important" on pages 283-285 and continued on page 292. He would welcome any comments any member of the York County Medical Society would wish to make.

An interesting highlight of this meeting was the election of Charles W. Kinghorn, M.D. of Kittery, to extend his tenure of office to thirty-eight years: truly a remarkable feat. It is interesting to note that he has never missed a meeting during all this time.

Approximately thirty-five were in attendance, including members and guests. The next meeting will be held at the Officers Club of the U.S. Naval Installation in Kittery on Tuesday, March 11, 1970. It was voted to have this an evening meeting on a trial basis to determine the extent of the participation of the York County Medical Society at an evening meeting. This meeting will be a combined effort of the Portsmouth Medical Club and our County. In charge of the program will be Dr. Kinghorn, representative of the York County Medical Society, who will assist Captain Russ Fisichello of the U.S. Naval Installation. Dr. Fisichello expressed a desire to have a roster of civilian consultants in various fields at the Naval Facility and urged all interested individuals to contact him.

An inquiry was made by the York County Community Action Corporation requesting the participation of one of the members of the York County Medical Society to serve on the Board of this Corporation. Another item of correspondence was from Richard C. Dillihunt, M.D., Chairman of the Maine Medical Search Committee, to obtain an Emergency Division Director. He requested that an announcement be made at our next meeting as to the availability of such an individual. In addition, he requested that anyone interested should contact him for details.

Three new members were elected to the York County Medical Society: Drs. Herman G. Sandvoss, Kennebunkport, William F. Wieting, York Harbor and Mahlon P. Palmer, Springvale.

During the closing moments of the meeting, Dr. Viger turned over the meeting to the incoming President, Maurice Ross, M.D.

CHARLES W. KINGHORN, M.D., *Secretary*
MELVIN BACON, M.D., *Assistant Secretary*

ANDROSCOGGIN

The Androscoggin County Medical Association met at the Central Maine General Hospital in Lewiston, Maine on January 15, 1970. The meeting was opened by the President, Lionel R. Tardif, M.D. with seventeen members present.

Philip L. Archambault, M.D. outlined the proper procedure to be followed if a patient has a complaint against a physician.

Charles W. Steele, M.D. mentioned the amount that physicians are to receive from Medicare this year.

Thomas F. Shields, M.D. felt the Association should go on record favoring notification by the intermediary to the physician in cases where the physician does not accept assignment of Medicare fee and patient is paid directly. This was voted on favorably and will be passed to the Insurance Committee.

The speakers of the evening were O. Thomas Feagin, M.D. and Charles H. Okey, Ph.D. who discussed rubella vaccine. Dr. Tardif thanked the speakers on behalf of the Association.

Lillian M. Hall, M.D. of Lewiston was elected to membership in the Association.

A meeting of the Androscoggin County Medical Association was held at St. Mary's General Hospital in Lewiston, Maine on February 19, 1970. The meeting was called to order by the President, Lionel R. Tardif, M.D. with twenty-nine members present.

A summary of the Diabetic week was read by E. Stanley Young, M.D.

Philip L. Archambault, M.D. brought up the question of sudden rise in malpractice rates and the Secretary was instructed to write to Daniel F. Hanley, M.D. requesting the number of malpractice suits in the State during the past year and the amount of money paid for these claims.

Charles W. Steele, M.D. read the latest information on Medicare assignment forms, Health and Welfare reports and letters concerning fee increase, (roughly 10% to keep up with cost of living), Social Security disability fee form and new fee profiles on Internists to be made in March.

Dr. Steele introduced the speaker, Charles F. Branch, M.D. of Auburn, President of the Maine Medical Association. Dr. Branch reviewed the problems confronting the medical profession in this day and age as brought out at the New York meeting. Some of the possible remedial steps were outlined and discussed. In all, the picture is not too bright. A question and answer period followed.

Dr. Tardif introduced our District Councilor, Charles W. Eastman, M.D. of Livermore Falls. He explained further the priorities as listed in the AMA Board of Trustees report on planning and development. The Maine Medical Association had a report with same objectives off the press last August. There is a move under foot to get younger men into the Council and take more active part in the State Medical Association affairs.

The members of the Association would like to know how many persons there are in the State who are not getting adequate medical care and how the figures are ascertained.

Cyprien L. Martel, Jr., M.D. reopened the discussion concerning discriminatory practice of physicians not being paid by Welfare Boards when all others are paid. After considerable discussion, it was moved and voted to have the chair appoint a committee to look into this matter. Point to be made is that the public be made aware that physicians aren't being paid.

The following officers were elected for 1970:

President, Lionel R. Tardif, M.D., Lewiston
Vice-President, Charles W. Steele, M.D., Lewiston
Secretary-Treasurer, Donald L. Anderson, M.D., Lewiston
Delegates to the M.M.A. House of Delegates, Drs. Lionel R. Tardif, Wilfrid A. Cloutier, Joseph J. Rando, John W. Carrier and Thomas F. Shields, all of Lewiston. Alternates, Drs. Charles W. Steele, J. Paul Nadeau, Daniel R. Shields, Cyprien L. Martel, Jr. and Ralph Zanca, all of Lewiston

DONALD L. ANDERSON, M.D., *Secretary*

PISCATAQUIS

A meeting of the Piscataquis County Medical Society was held at the Squaw Mountain Ski Area Lodge in Greenville, Maine on January 21, 1970 with thirty-eight members and guests present.

After an excellent dinner, Clement A. Hiebert, M.D. of the Maine Medical Center took us on a "Medical Safari" on the S.S. Hope. Dr. Hiebert was a very interesting speaker and his program was enjoyed by all of us.

O. Thomas Feagin, M.D. of the Communicable Disease Division of the State Health Department spoke to us about the

immunization program of German Measles Vaccine to be given all females up to twelve years of age.

At our regular meeting, Edwin T. Wyman, M.D. of Bowerbank, Maine and Brookline, Massachusetts was elected to membership in the Society.

It was unanimously passed that Linus J. Stitham, M.D. would present a resolution at the M.M.A. House of Delegates interim meeting in Brunswick, Maine on April 5, 1970 relative to osteopaths.

ISAAC NELSON, M.D., *Secretary*

LINCOLN-SAGADAHOC

The Lincoln-Sagadahoc County Medical Society met at The Ledges on January 20, 1970.

The minutes of the last meeting were read and accepted. The treasurer's report was read as written and accepted with the suggestion that dues be lowered to $25.00 next year.

It was voted that this Society donate $100.00 to the State of Maine Caddies' Scholarship Fund in recognition of the interest of Dr. Francis A. Winchenbach in this fund.

Charles E. Burden, M.D. reported that Bath has 400 doses of rubella vaccine available for school children.

John F. Andrews, M.D. reported for the nominating committee the following slate of officers for the coming year:

President, Arkadij Oceretko, M.D., Bath

Vice-President, Frank O. Avantaggio, Jr., M.D., Damariscotta

Secretary-Treasurer, George W. Bostwick, M.D., Newcastle

Delegates to the M.M.A. House of Delegates, Drs. Nelson P. Blackburn, Bath and Mary J. Tracy, Damariscotta. Alternates, Drs. Richard Evans, III, Wiscasset and Alfred T. Holt, Bath

Censors, Drs. John F. Dougherty, Bath, Carl R. Griffin, Jr., Boothbay Harbor and Samuel L. Belknap, Damariscotta

Program Committee, Drs. Henry A. Hudson, Southport Island and Nelson P. Blackburn, Bath

The slate was accepted and the Secretary instructed to cast one ballot for the slate.

Dr. Bostwick read a discussion of relations between the osteopathic and allopathic professions. Dr. Griffin moved that the Council members, delegates, and alternates be instructed to support the concepts outlined in the report by Dr. Bostwick; that all barriers to association be dropped. Dr. Burden seconded the motion which was passed without dissent.

A regular meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on February 17, 1970. The meeting was called to order by the President, Arkadij Oceretko, M.D.

Dr. Bostwick read a request from the Maine Medical Association for the names of members interested in serving on M.M.A. special committees and standing committees. He then abstracted "Report I of Board of Trustees of the AMA, by the Committee on Planning and Development."

Nelson P. Blackburn, M.D, introduced Robert P. Timothy, M.D. who spoke on Pediatric Urology.

GEORGE W. BOSTWICK, M.D., *Secretary*

WASHINGTON

The regular meeting of the Washington County Medical Society was held on February 23, 1970 at the Eastport Library, Eastport, Maine with eight members and guests present.

The meeting was entirely a business meeting under the direction of G. Bernard Shaw, M.D., President. The reading of the minutes of the last meeting were dispensed with.

The Prescription Vendor program for public assistance patients was discussed. No action was taken. James C. Bates, M.D. of Eastport then discussed the Regional Medical Program. He has been attending meetings for the last eight months, usually held in Augusta. He stated that speakers would be available for county and staff meetings from the Bangor area. Dr. Bates discussed some of the various programs that the Regional Medical Program is trying to set up. He stated that the Penobscot Valley Regional Health Agency had been organized, that also a Washington County Regional Health Agency had been set up, but the bylaws as yet had not been completely formulated.

The Secretary was asked to write to Frances Brown, Calais who is on the committee to formulate the bylaws.

Dr. Shaw read a telegram from the Department of Health and Welfare advising that the MIC Program would not accept new patients after 5:00 p.m. Friday, February 27, 1970. The members were advised that there would be an interim meeting of the House of Delegates on Sunday, April 5, 1970 at Brunswick, Maine.

KARL V. LARSON, M.D., *Secretary*

HANCOCK

The January meeting of the Hancock County Medical Society met at the Mount Desert Island Hospital Extended Care Unit in Bar Harbor, Maine with thirteen members and eleven guests present.

A tour of the Extended Care Unit was carried out by Mr. Meriweather, the Physical Therapist, showing the Therapy Unit he designed for his use and an Occupational Unit, as well as the twenty-six patient beds, all of which were much admired.

During the business meeting, after reading of the minutes and their approval and other correspondence, an announcement of old business in the form of the Family Planning Clinic to be held at the Blue Hill Memorial Hospital, January 26 was mentioned and a request for information by the Diabetes Chairman, John C. Van Pelt, M.D. was made.

Under new business, Drs. John R. Hewson of Southwest Harbor and Kendall A. Gerdes of Northeast Harbor were accepted into membership, and endorsement was made by the membership of the Kidney Dialysis Unit at the Maine Medical Center (support through legislation being considered by the 104th State Legislature through a letter from the County Society Secretary), and a discussion of the acceptance of Osteopathic physicians at County Society meetings.

The speaker of the evening was Richard T. Chamberlin, M.D., Director of Rehabilitation Service at the Thayer Hospital, who commented on the experience at that institution with certifying Extended Care to the Medicare Administrators in Portland. His address emphasized the importance of concise, pertinent admission notes, progress notes and prognosis for patients being transferred to Extended Care. These notes and the nurses notes are used by the Administrators to justify utilization and therefore payment for care by the Medicare office. Acceptance was no problem where the records showed the indicated care was ordered for certain indications and was carried out with a certain anticipated result in the rehabilitating of the patient. The ensuing discussion brought out Dr. Chamberlin's belief that such record keeping should be a part of the patients' care in the continuing from Acute to Extended to Outpatient Care whether or not the Medicare Administration was involved to insure good patient care and the utilization of facilities. A heated discussion involved what these records should be and who should be using them to determine whether care should be paid for or not. The meeting was adjourned after a most interesting and enlightening program concerning this new facility available in Hancock County.

The Hancock County Medical Society meeting was held at the Maine Coast Memorial Hospital in Ellsworth, Maine on February 11, 1970 with thirteen members and ten guests present.

Support by the 104th Legislature of the Hemodialysis Unit at the Maine Medical Center was noted pertinent to the letter that the Secretary was instructed to send to our local legislative representatives recommending support of this proposal.

Rowland W. Pritchard, M.D., U.S. Naval Reserve, Naval Security Group, Winter Harbor, Maine was accepted to membership of the Society.

A message from O. Thomas Feagin, M.D. of the Communicable Disease Control Division of the Department of Health and Welfare, regarding the rubella prevention campaign in Maine, was read.

Robert F. Russell, M.D. reported on Maine Medical Association Council business, noting the advance of the Maine Medical Education Foundation both in terms of funds and those numbers of students assisted by loans. He noted that a dues increase seems likely.

Pertinent to the resolution on the acceptance of osteopathic physicians, it was noted that Dr. Paul Cushman, Dr. Bernard Berry and Dr. Donald Gagnon had accepted invitations to attend this evening's meeting. Also, Dr. Edward T. Newell from the Osteopathic Hospital of Maine in Portland was one of the speakers of the evening, giving an address on the use of TV in continuing medical education. Mr. Hopkins, from the ETV Station in Orono, commented on his experience and future plans for Instructional TV in Maine. Dr. and Mrs. Weiswande were introduced as visitors to the Mount Desert Island Hospital as part of the Bingham Foundation Guest Resident Program.

BRADLEY E. BROWNLOW, M.D., *Secretary*

KNOX

The following officers were elected for 1970:
President, Johan Brouwer, M.D., Rockland
Vice-President, Henry O. White, M.D., Rockland
Secretary-Treasurer, Alan F. Woodruff, M.D., Rockland

RICHARD D. WATERMAN, M.D., *Secretary*

News, Notes and Announcements

State of Maine Board of Registration of Medicine
Secretary — George E. Sullivan, M.D.
Waterville, Maine
Physicians Licensed to Practice Medicine and Surgery in the State of Maine
June 20, 1969

Through Examination

Sallah U. Abbasey, M.D., 190 Sunset St., Wilson, N.Y.
Eleuterio S. Alilin, M.D., Mercy Hosp., Portland, Me.
Dushan J. Babich, M.D., Lutheran Med Ctr., Brooklyn, N.Y.
Ali Chinichian, M.D., 513 Oakdale Rd., East Meadow, N.Y.
Eugenio B. Chua, M.D., 125 Ashland Place, Brooklyn, N.Y.
Mehmet A. Eragan, M.D., The Regency Apts., Winterhaven, Fla.
Fakhreddin Entezary, M.D., Roger William Gen. Hosp., Providence, R.I.
Malcolm C. Fairweather, M.D., Mercy Hosp., Portland, Me.
Atilio B. B. Giangreco, M.D., 300 Longwood Ave., Boston, Mass.
Ramon T. Guiao. M.D., 20073 Lorain Rd., Fairview Pk., Ohio
Mokarram H. Jafri, M.D., Taunton State Hosp., Taunton, Mass.
Ganapathy K. Kumar, M.D., 16216 W. 13 Mile Rd., Birmingham, Mich.
Emil M. Laga, M.D., 305 Memorial Dr., Cambridge, Mass.
John Mathews, M.D., 2760 Victory Blvd., Staten Island, N.Y.
Eladio T. Menorca, M.D., 269 Meadowlawn Rd., Cheektowaga, N.Y.
Manouchehr Michael, M.D., New Rochelle Hosp., New Rochelle, N.Y.
Augusto E. Midolo, M.D., 25 Newton St., Brighton, Mass.
Victor G. Millan, M.D., 111 Perkins St., Boston, Mass.
Kazem Motiey, M.D., 19500 Euclid Ave., Cleveland, Ohio
Michael D. Murphy, M.D., 53 Hancock St., Boston, Mass.
Abolhassan Pourhamidi, M.D., 11 Cogswell Ave., Cambridge, Mass.
Eshmail M. Sarkis, M.D., 961 Victory Blvd., Staten Island, N.Y.
Jorge E. Secchi, M.D., 223 F Oceanview, Ft. Hamilton, Brooklyn, N.Y.
Milan S. Smolko, M.D., Harrisburg State Hosp., Harrisburg, Pa.
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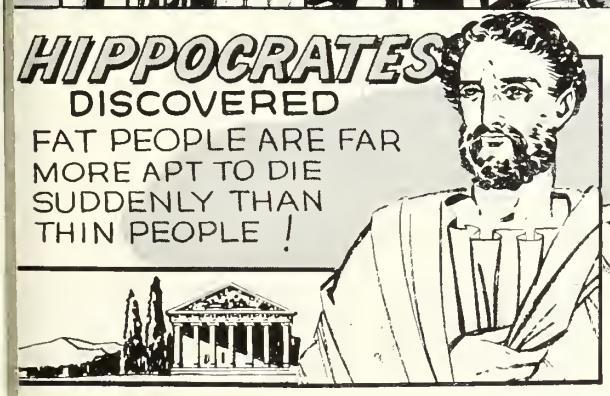

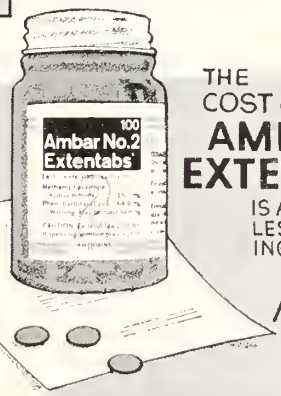

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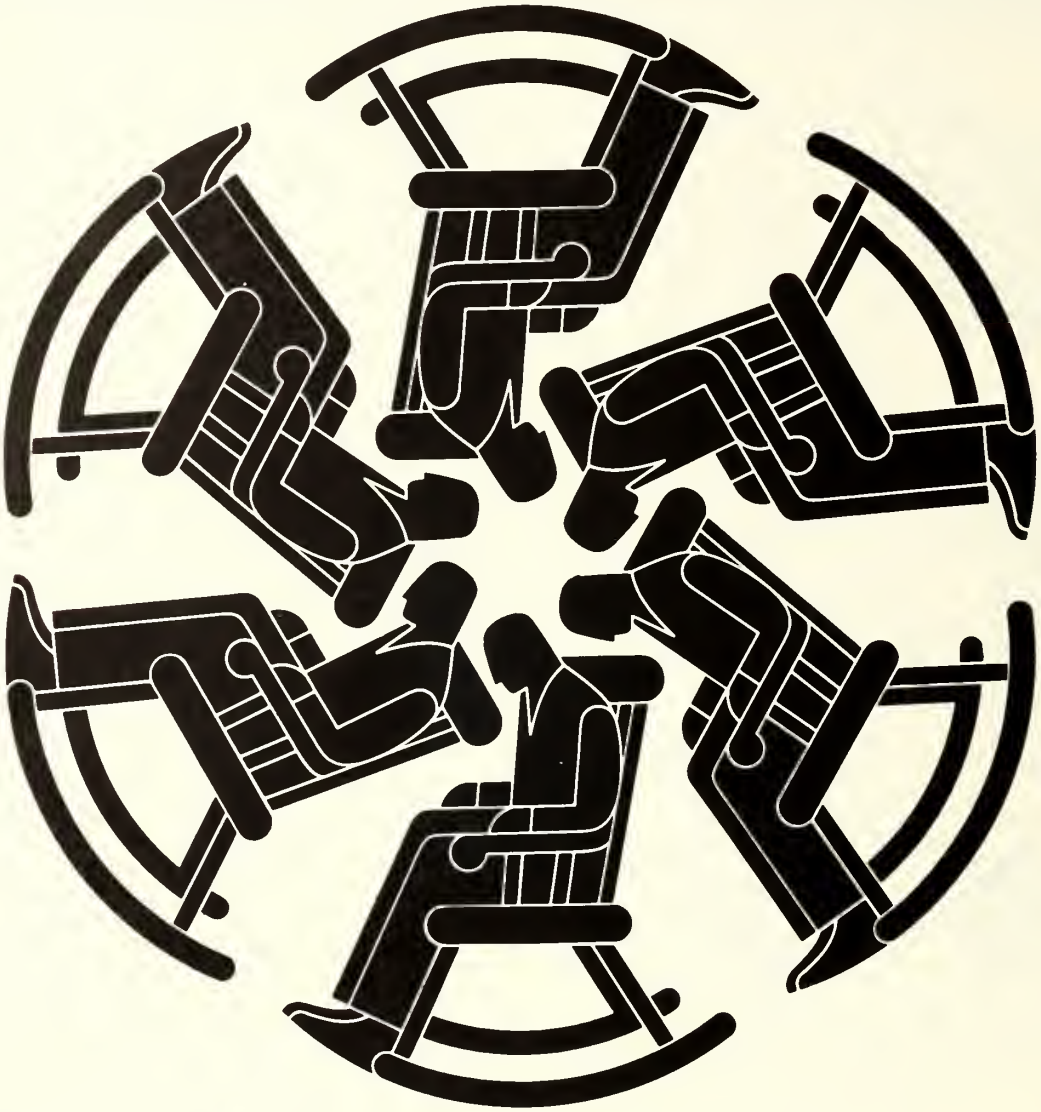

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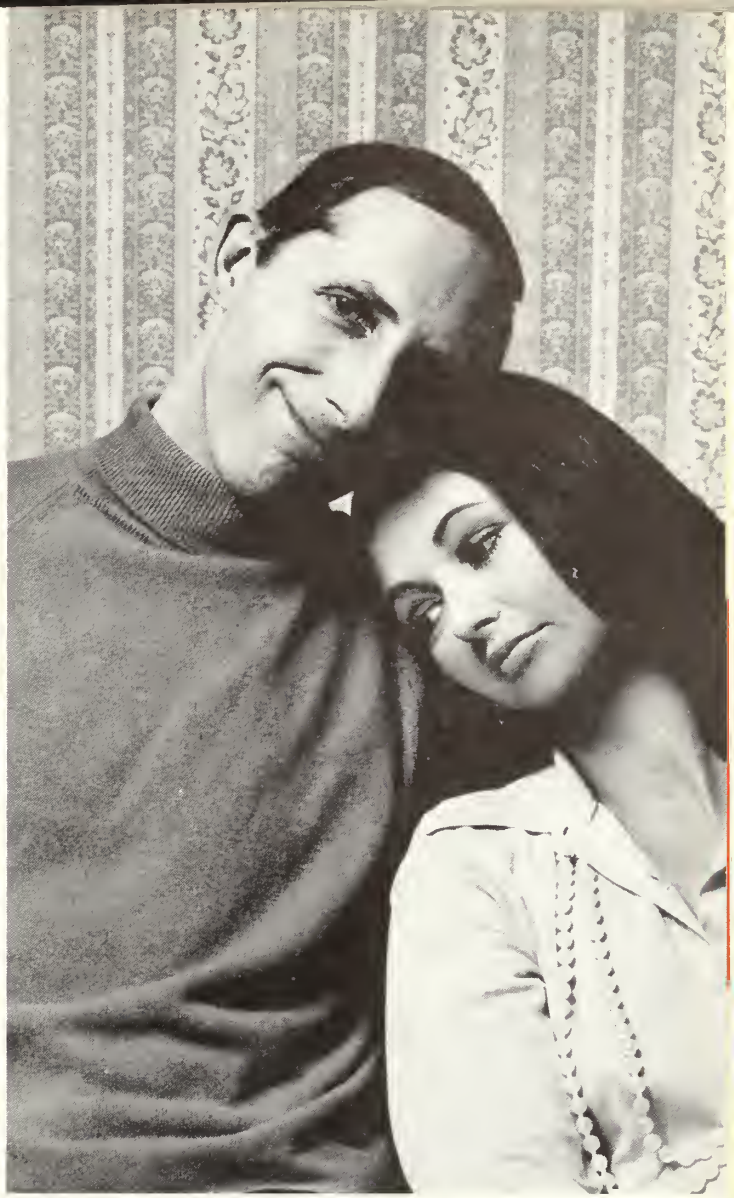

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.*: Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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1. Kannel, W.B., *et al.*: *Circulation* 35:734, 1967.
2. Thomas, H.E., Jr., *et al.*: *Med. Times* 95:1099, 1967.
3. Albrink, M.J., in: Beeson, P.B. & McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Phila.: W.B. Saunders Co., 1967.

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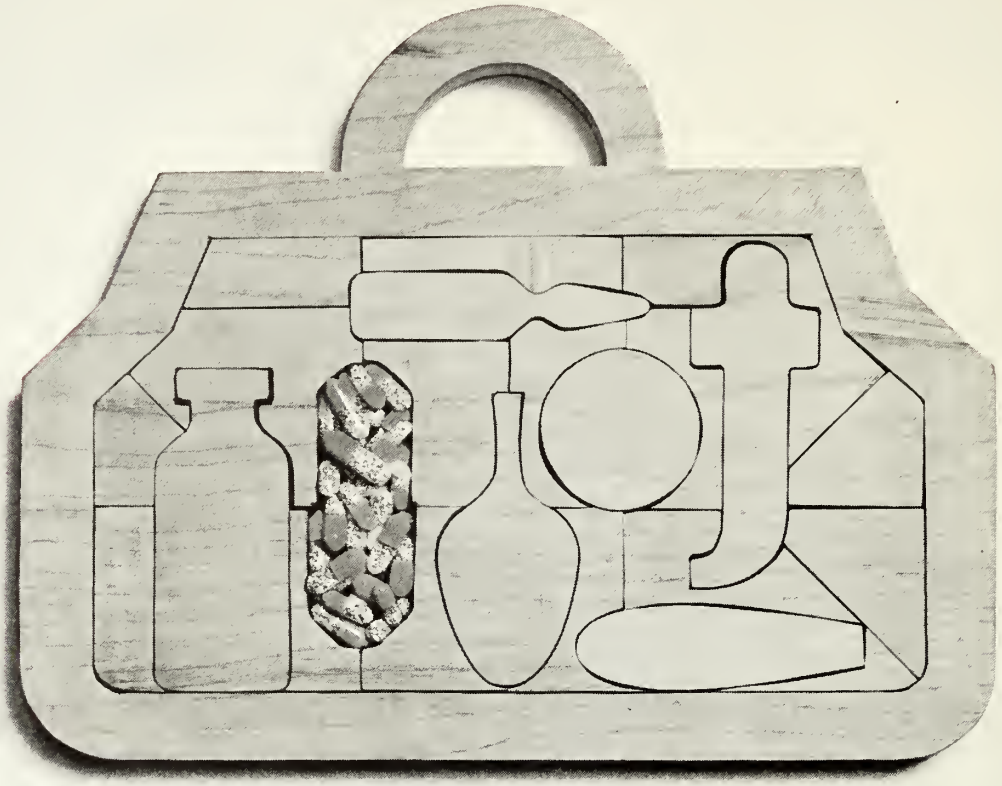

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Schuyler, Oct. 31. Harry Waters of Covesville incurred a fractured arm ... acht ... ck a large rock tially capsized. The fire depar had to rescue Waters by smal Damage to the yacht is estima

Hasn't the skipper had enough excitement for one day?

For the patient who has been through an accident, the worry and anxiety following the mishap may actually heighten the perception of pain. This is why there's a classic ¼ grain *sedative* dose of phenobarbital in Phenaphen with Codeine—to take the nervous "edge" off, so the rest of the formula can control the pain more effectively.

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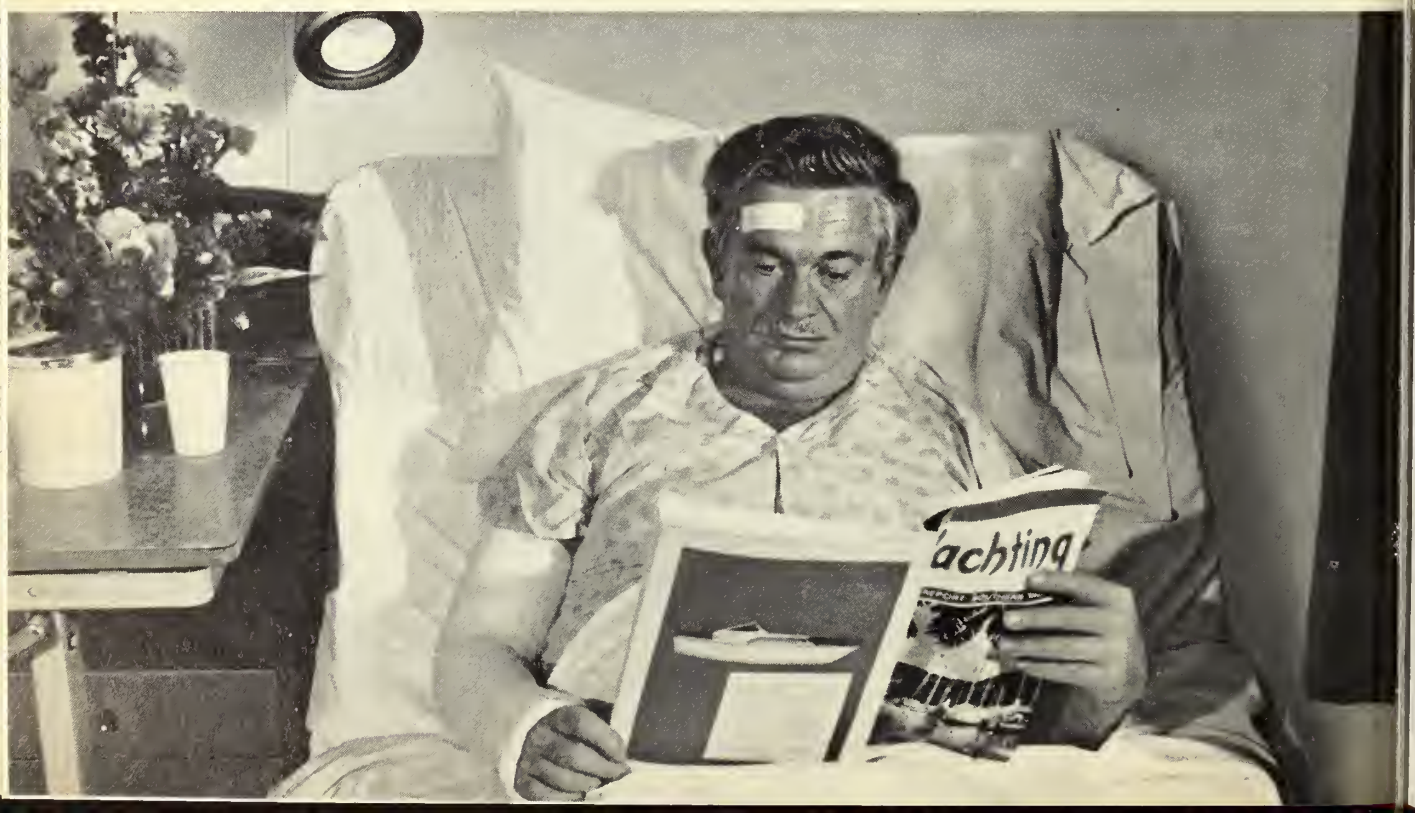
Phenaphen with Codeine Nos. 2, 3, or 4 contains: Phenobarbital (¼ gr.), 16.2 mg. (warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Hyoscyamine sulfate, 0.031 mg.; Codeine Phosphate, ¼ gr. (No. 2), ½ gr. (No. 3), or 1 gr. (No. 4) (warning: may be habit forming).

The compound analgesic that calms instead of caffeinates

Indications: Phenaphen with Codeine provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.



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In Witness Whereof Associated Hospital Service of Maine (a Non-profit Maine Corporation) has duly executed this Contract.

Countersigned by:

President — *Chairman of the Board*

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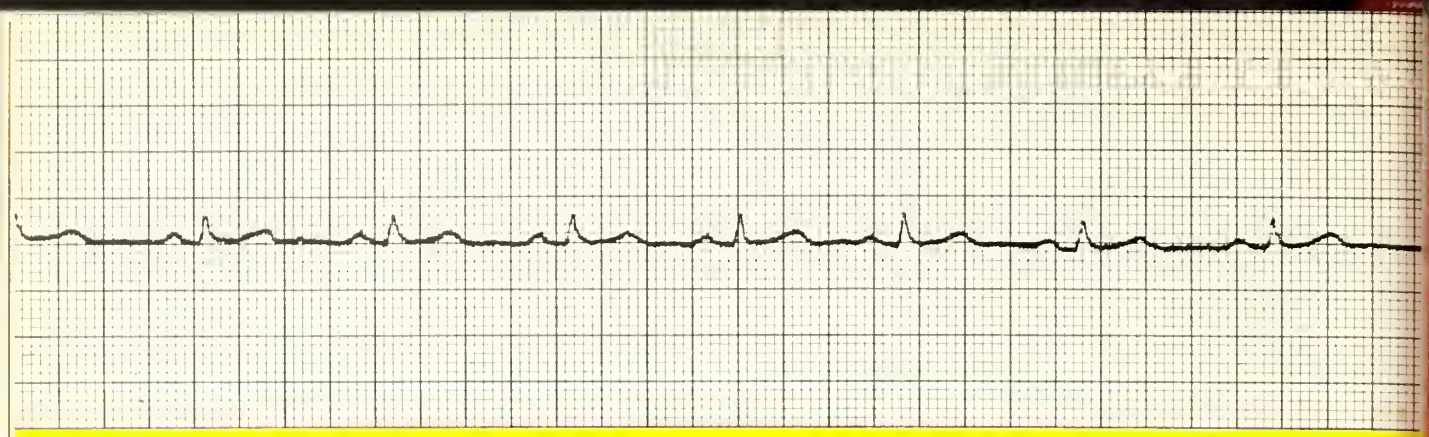

When disease is ruled out and psychic tension is implicated

Valium® (diazepam)

helps relax the patient and relieve his somatic symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation: acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms have occurred following abrupt discontinuance. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation, have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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1970 Annual Session — June 7, 8, 9
The Colony, Kennebunkport
Program In This Issue

ROBERT L. OWLETT, M. D.
BOX 42, WHITTIER AVE.
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THE JOURNAL
of
The Maine Medical Association

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* ESTHER M. KENNARD, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.

Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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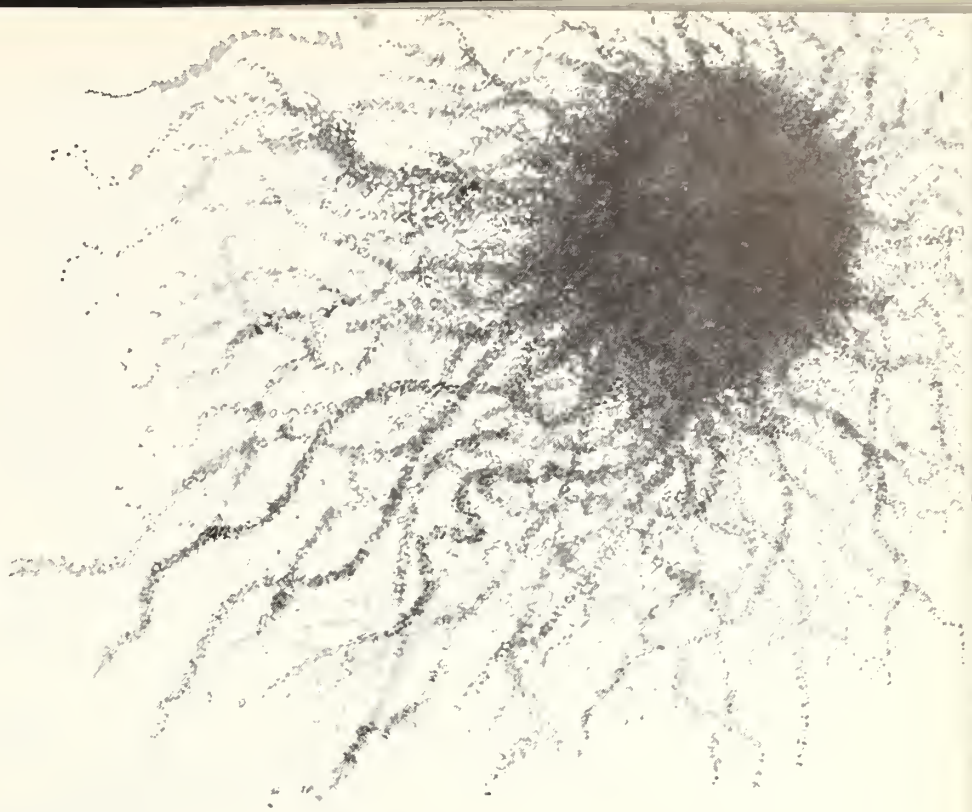

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then antibiotic therapy last week.

and monilial overgrowth this week.

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Warning: In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

Precautions: Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects: Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose-related. Transient, reversible, nephrogenic diabetes insipidus with excessive thirst and polyuria (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth—dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy. Demethylchlortetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.

Average Adult Daily Dosage: One tablet b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

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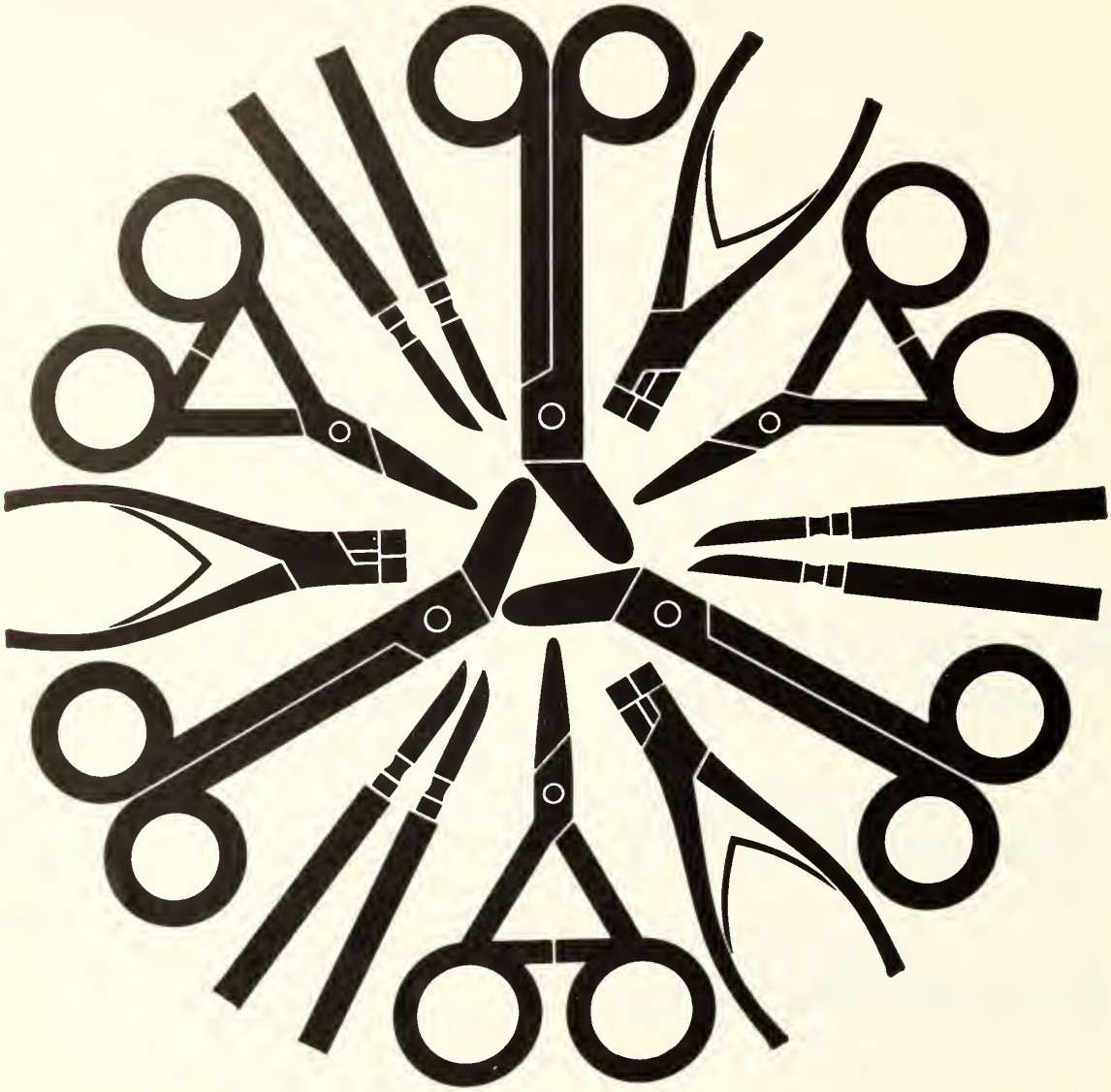
before and after surgery



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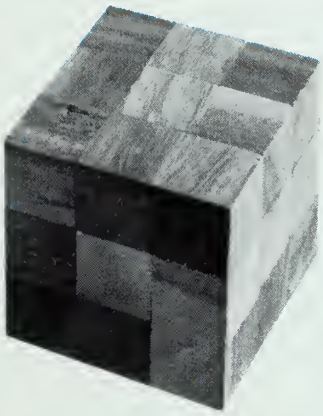

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Effects: Rapid relief of pain, relaxation of smooth muscle spasm through parasympatholytic action of atropine and hyoscyamine; pus cell content decreased.

Administration and Dosage:

Adults: Two tablets, orally, four times per day, followed by liberal fluid intake.

Children: One-half the adult dose.

Acute cases: Initially two tablets every hour for three doses, followed by the recommended daily administration.

Precautions: Administer with caution to persons with known idiosyncrasy to atropine and cardiac disease. While under this therapy the urine is blue; patients should be so advised to allay apprehension.

Side Effects: Neither irritation nor untoward reactions have been reported; however, if pronounced dryness of the mouth, flushing, or difficulty in initiating micturition occurs, decrease dosage. If rapid pulse, dizziness or blurring of vision occurs, discontinue use immediately. Acute urinary retention may be precipitated in prostatic hypertrophy.

Contraindications: Glaucoma, urinary bladder neck or pyloric obstruction, duodenal obstruction and cardiospasm. Hypersensitivity to any of the ingredients.

How Supplied: Bottles of 100, 500 and 1,000 tablets.

References: (1) Sands, R. X.: New York St. J. Med. 61:2598-2602, 1961; (2) Renner, M. J., et al.: Hosp. Topics 39:71-73, 1961; (3) Haas, Jr., J., and Kay, L. L.: Southwest. Med. 42:30-32, 1961; (4) Marshall, W.: Clin. Med. 7:499-502, 1960; (5) Strauss, B.: Clin. Med. 4:307-310, 1957.

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The neighbors are wonderful.

Indications. For use in management of anxiety and tension occurring alone or as accompanying symptom complex to medical and surgical disorders and procedures. Though not a hypnotic, fosters normal sleep through antianxiety and related muscle-relaxant properties.

Contraindications. History of sensitivity to meprobamate.

Important Precautions. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics. After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures.

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination.

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery.

Side Effects include drowsiness, usually transient; if persistent and associated with ataxia, usually responds to dose reduction; occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin. Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone. Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration.

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(meprobamate)

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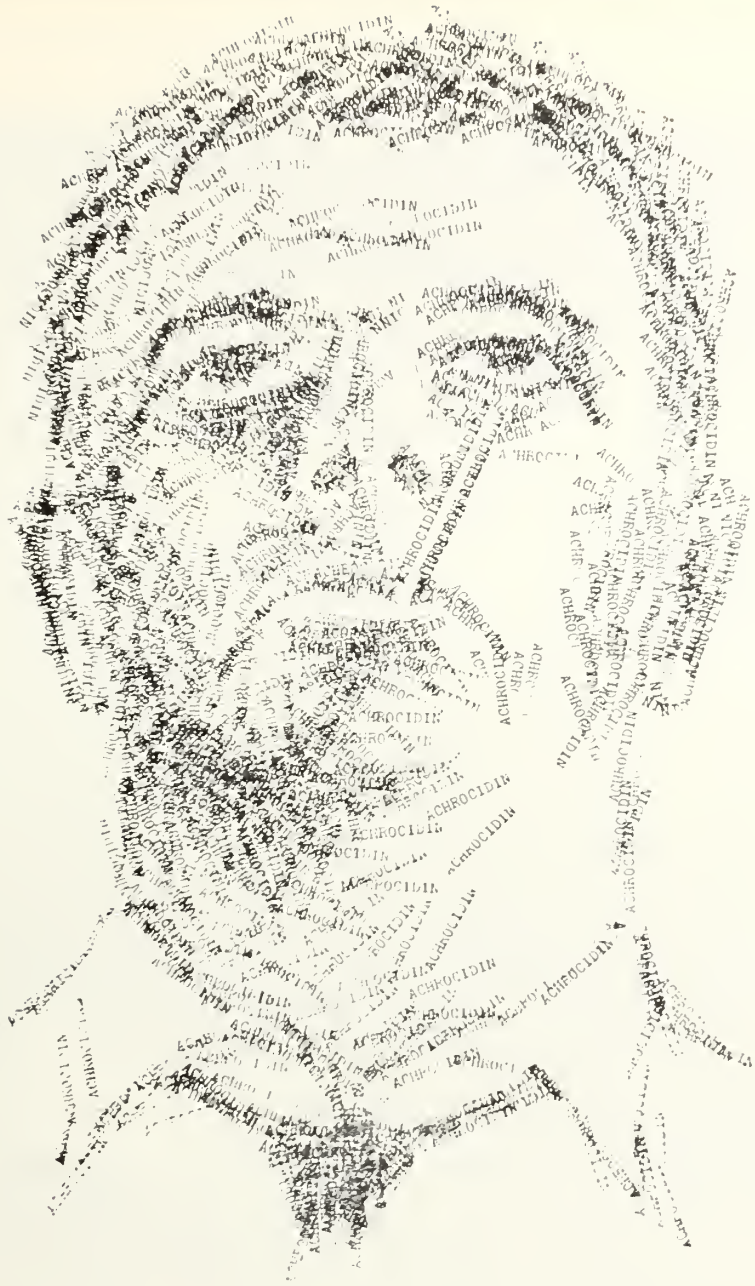

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traindications: Hypersensitivity to any ponent.

ning: In renal impairment, since liver tox- is possible, lower doses are indicated; dur- prolonged therapy consider serum level rminations. Photodynamic reaction to sun- t may occur in hypersensitive persons. osensitive individuals should avoid expo- ; discontinue treatment if skin discomfort rs.

autions: Drowsiness, anorexia, slight gas- distress can occur. In excessive drowsi- , consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

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The Journal
of the
Maine Medical Association

Volume Sixty-one | Brunswick, Maine, May 1970 | Number 5

Nursing and Medicine

WILLIAM L. MACVANE, JR., M.D.,* GUEST EDITOR

As we enter the 1970's, it should be clear to even the most obtuse that change is the order of the day. In no fields is this more evident than in Nursing and Medicine. Both professions are faced with changes in demands by the public and changing curricula in their schools.

Nursing arose as a modern profession somewhat over one hundred years ago following the Crimean War. After this, the "Training School Era" lasted through World War II. During this period, nurses were treated in a somewhat paternalistic fashion by the medical profession as exemplified by the writings of Sir William Osler. Next came the "Period of Educational Emphasis and the Accreditation of Nursing Schools." This was followed by closure of innumerable marginal diploma schools and the propagation of university and associate degree nursing programs. This latter phase could be likened to the changes brought about in medical education by the Flexner Report in the early years of this century.

Now both professions are faced with countless changes which may or may not be to their advantage. These changes must be studied and carefully evaluated to insure that change is made only in the public interest and for better patient care. The advent of Schools of Allied Health Professions with their many programs such as physician assistants opens new problems of professional accreditation, licensing, liability, etc. In fact, the executive director of the Canadian Nurses Association sees the nurse of 1980 as a family practitioner whose main concern is health.[1]

The whole point of this perhaps wordy editorial is to state that in Maine we have had a Nurse-Physician Liaison Committee of the Maine Medical Association and the Maine State Nurses Association since 1962. Its greatest accomplishment so far, perhaps, has been to keep lines of communication open, to establish rapport, and the development of mutual respect for committee members and their points of view.

As co-chairman of this committee, I feel, as does the rest of the committee, that the time has come when a Nurse-Physician Conference on our common problems should take place yearly either at the Maine Medical Association annual meeting, the annual meeting of the Maine State Nurses Association, or a separate special meeting. I personally would favor alternate meetings at the Maine Medical Association and the Maine State Nurses Association for this purpose.

The AMA encourages such state-wide conferences; the times demand them. Nurses and physicians meeting as equal partners in a conference of this type can provide a very comprehensive view of the delivery of health care services in our State and avoid the types of unilateral pronouncement and action which create misunderstandings.

REFERENCE

1. Mussallem, H. K., *The Changing Role of the Nurse.* A.J.N. 69; 514, 1969.

*Director of Medical Education, Mercy Hospital; Chairman, Maine Medical Association – Maine State Nurses Association Nurse-Physician Liaison Committee.

Ureteral Colic Heralding Vesico-Ureteral Reflux‡

ROBERT P. TIMOTHY, M.D.* and ALAN D. PERLMUTTER, M.D.**

Vesico-ureteral reflux is a well documented finding in many cases of recurrent urinary tract infection; it may result in ureteropyelocalyceal decompensation and atrophic pyelonephritis. With cinefluorography and cystography the detection of significant reflux rarely presents a problem. This case of a young boy with unilateral reflux, occurring only during micturition, is presented to underline the necessity of eliciting a complete history, and then obtaining adequate studies to demonstrate the pathology and its etiologic mechanisms.

CASE REPORT

M. H.: (C.H.M.C. NO. 60-93-96) – This white male, aged five and one-half years, was admitted to Pediatric Service in April of 1966 with a two-day history of fever to 104° F., chills, nausea, and vomiting. At that time, a vague history of right flank pain for the previous year was elicited. Urine culture grew out Escherichia Coli, 20,000 colonies per milliliter of urine. The patient was treated with a two week course of sulfisoxazole, 0.5 gm. every six hours with a defervescence of fever over a two-day period.

Voiding cystourethrogram on April 25, 1966, (Figure 1B) showed no evidence of reflux; voiding and postvoiding films were not obtained. Intravenous urogram at that time (Figure 1A) was interpreted as normal.

In July of 1966, off chemotherapy for four weeks, the patient experienced urinary frequency and dysuria, and urine culture grew significant Streptococcus Fecalis. He was restarted on sulfisoxazole, 0.5 gm. q.i.d. and maintained on this therapy without further evidence of urinary infection.

In August of 1966, he was re-admitted with right lower quadrant and right low back pain, during and immediately following micturition, radiating into the right groin and thigh. The parents recalled that the patient had had similar complaints for approximately eighteen months.

On physical examination, temperature was 98° F., blood pressure was 110/60, and weight was in the 75th percentile for his age. No localizing abnormalities were detected. Urinalysis contained no protein, and no cells; and urine culture had no growth of bacteria. BUN was 17 mg. percent.

Intravenous urogram (Figure 2A) on August 11, 1966 showed delayed visualization and diminished concentration of contrast material on the right, and the renal outline was obscured. Voiding cystourethrogram (Figure 2C) showed total right vesico-ureteral reflux present only on voiding, with marked upper tract dilatation. At cystoscopy, there was no evidence of urethral or bladder neck obstruction. Mild chronic cystitis was observed, with moderate ectopia lateralis of both ureteral orifices. The left orifice had a normal configuration, and the right appeared patulous. To further evaluate right renal function and size, a Neohydrin 197 renal scan (Figure 2B) was performed, which showed the right kidney to be approximately two-thirds the size of the left, an apparent change from the size noted on the initial excretory urogram of April, 1966.

Because of massive right vesico-ureteral reflux with evidence of atrophic pyelonephritis, a right ureteroneocystostomy (reimplant) was performed on August 15, 1966. The patient had a smooth postoperative course. He was discharged from the hospital on the seventh postoperative day on chemotherapy. Postoperative BUN was 9 mg. percent, and urine culture showed no growth of bacteria.

Postoperatively, his urine has remained uninfected off sulfisoxazole therapy. Intravenous urogram at two weeks and six months (Figure 3A) following reimplantation showed no change in the right calyceal deformity and parenchymal atrophy, and no evidence of right vesico-ureteral obstruction; a cystogram showed no reflux. A Neohydrin 197 renal scan obtained six months following reimplantation is unchanged from the postoperative study.

DISCUSSION

Vesico-ureteral reflux may occur at any time during filling or emptying of the bladder. Low pressure reflux may be defined as that occurring during the isotonic horizontal slope of the normal cystometrogram; this usually implies bladder pressures of less than 15 to 20 cm. H_2O. High pressure reflux occurs when the intraluminal bladder pressure exceeds 25 to 30 cm.H_2O, and in the normally innervated bladder this is temporally concurrent with urinary urgency. Low pressure reflux is occasionally seen only during initial filling of the bladder and paradoxically disappears with elevated bladder pressure or volume. Vesico-ureteral reflux seen only on voiding is

Fig. 1A

Fig. 1B

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**Clinical Associate in Surgery, Harvard Medical School; Associate in Surgery (Urology), Children's Hospital Medical Center, Boston, Massachusetts.

Fig. 2A

Fig. 2B

Fig. 2C

not common, and may be explained by the increased intravesical pressure of micturition associated with a marginally competent uretero-vesical junction.

The right abdominal and back pain noted by this boy occurred only during voiding, and acute ureteral dilatation was seen with the "voiding reflux." Ureteral distention may result in ureteral colic. Hutch[1] briefly refers to patients who complain of renal pain during voiding and who have reflux.

Voiding reflux is most often seen as an evanescent phenomenon without distention of the ureter or collecting system. This case documents that significant upper tract dilatation and serious upper tract damage may occur in association with vesico-ureteral reflux occurring only during voiding.

Fig. 3A

Summary

Ureteral colic during and immediately following micturition has been described, in association with severe vesico-ureteral reflux occurring only during voiding. The various circumstances of reflux are discussed. The necessity for an adequate history and modification of the diagnostic evaluation to provide maximal information is emphasized.

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Pyoderma Gangrenosum Following Minor Trauma

EUGENE P. MCMANAMY, M.D.,* MALCOLM C. FAIRWEATHER, M.D.** and DAVID E. KEEN, M.R.C.S. (Eng.)***

Pyoderma gangrenosum is an unusually severe purulent ulceration of the skin.[6] It is a rare condition, less than one hundred cases having been reported. Mayo Clinic studies of 62 patients between 1955 and 1967 showed that 50% have chronic ulcerative colitis, as well as 40% of patients with other underlying disease. There was evidence of trauma as a precipitating factor in 20% of these patients and in a further 50% trauma was also suspected in patients who had no other identifiable disease. The condition mainly occurs in the 30-40-year old age group and females were found to be more often affected than males.[1] The associated diseases mentioned were ulcerative colitis, empyema, arthritis, regional ileitis, peptic ulcer, diverticulitis and perforated appendicitis.[3,6]

It is suggested that there are three etiological types.

1. Violent antigen antibody reaction analogous to the Schwartzman phenomenon with associated hypogammaglobulinemia, altered plasma proteins and elevated blood sugars in some cases.
2. Brunsting type of intractible ulceration with gangrenous margins and irregular underlying sinuses exuding purulent material and associated with chronic disease.
3. Meleney type of ulceration of bacterial origin experimentally shown to occur in the presence of Beta hemolytic Streptococci in conjunction with coagulase positive Staphylococci infection and again associated with generalized systemic disease.[2,3,4]

The characteristic description of the disease is:

1. Early lesion often due to minor trauma, burn, abrasion, insect bit, etc.
2. Development of vesicle or pustule.
3. Painful ulceration with an inflammatory halo.
4. The classical development of a blue line or margin around the edge of the vesicle.
5. Undermined edges of the ulcer.
6. Spread by sinuses tracking under the skin to affect surrounding areas and the formation of new ulcers.
7. Coalescing to produce gross destruction of skin and subcutaneous tissue.
8. The presence or absence of generalized toxic reaction.[3,4]

The disease is classically resistant to healing with topical or systemic antibacterials, recurs after excision and frequently rejects autogenous skin grafts.[2] It has been most successfully treated with:

1. Dermabrasion.
2. Aqueous 0.5% silver nitrate soaks.
3. Corticosteroids with or without systemic bacterials.
4. Autogenous skin grafting.

Maintenance corticosteroids are necessary to maintain regression.[2,3,4]

REVIEW

Case Report: Fifty-one year old, white female admitted to hospital on August 11, 1969 with a history of minor trauma two days prior to admission, when she was struck by a small piece of wood thrown by her nephew, causing a small abrasion to the anterior part of the leg.

One day prior to admission she had difficulty in walking because of pain in her right calf and tense red swelling of the right lower leg. Her leg had become increasingly painful and the swelling had spread to the lower anterior thigh. She had noted some chills on the day prior to admission.

Past Medical History: No known diabetes or cardiopulmonary disease. No known bowel disturbances. Cholecystectomy two years prior to admission.

Personal History: Widow. Heavy cigarette smoker for many years. No known allergies.

Family History: No cardiopulmonary disease or diabetes.

Physical Examination: On admission, temperature 100.6 orally. Pulse 120, regular. Respiration rate 20. Blood pressure 130/90. Chest: Sparsely scattered low and high-pitched rhonchi over both lung fields. Abdomen: Healed right subcostal incision. Extremities: There were two small abrasions on the right lower anterior leg and marked pitting edema and cellulitis of the lower leg and anterior thigh. There was tenderness along the right deep calf and femoral veins and small tender lymph nodes in the right groin. No other peripheral lymph nodes were palpable.

The admitting diagnosis of cellulitis and lymphangitis of the right leg with question of deep calf vein thrombosis was made.

Laboratory Studies: Admission Hgb. 16 grams. White blood count 26,000 total; polys 86, lymphs 14. Urinalysis normal. Subsequent fasting blood sugar 162 mg.%. Glucose tolerance test showed diabetic type curve. Blood cultures repeatedly negative. Wound culture, initial, Alpha Streptococci, Pneumococci and E. Coli, resistant to Penicillin and Ampicillin; sensitive to Streptomycin and Tetracycline. Subsequent, Beta hemolytic Streptococci, Strep faecalis and Aerogenes, sensitive to Kantrex® and Chloramphenicol. Hgb. 16 grams. White blood count falling to 12,700; polys 64%, lymphs 35%, monocytes 1%. Corrected ESR 46 mm. per hour. BUN 17 mg.%. Serum calcium 10 mg.%. Phosphorus 4.1 mg.%. SGOT 37 units. LDH 1245 units. Total protein 6.8 grams%. Albumin 4.2 grams. Globulin 2.6 grams. Cholesterol 214 mg.%. Uric acid 5 mg.%. Total bilirubin 0.5 mg.%. Alkaline phosphatase 1.6 sigma units. Agarose electrophoresis was consistent with a chronic disease and acute inflammatory process with a low Alpha globulin of uncertain etiology. Antinuclear antibody titer was negative. EKG was normal. Chest x-ray studies showed old rib fractures and changes suggestive of chronic bronchitis.

*Chief of Surgery, Mercy Hospital, Portland, Maine 04101.
**Courtesy Staff, Surgeon, Mercy Hospital, Portland, Maine 04101.
***House Officer, Mercy Hospital, Portland, Maine 04101.

Treatment: (Initial) Bed rest, leg elevation, warm saline packs and Penicillin therapy were instituted.

(Subsequent Treatment) Following laboratory studies, bed rest, leg elevation, cold saline soaks, Streptomycin and Tetracycline, 1200 calorie ADA diet and Diabinese 500® mg. b.i.d.

Hospital Course: She apparently improved, her diabetes being well controlled, her temperature reverting to normal and the swelling subsiding until the 4th day following admission when blistering was noted, these blisters having a peripheral bluish hue. The skin began to slough and the blisters to break down revealing necrotic ulceration distal to the main area of sloughing over the whole of the anterior and lateral parts of the lower leg above the ankle. At this point, the diagnosis of pyoderma gangrenosum was made. Subsequent to this and further laboratory studies listed above, the following regimen was instituted.

1. Silver nitrate soaks using 0.5% silver nitrate.
2. Kantrex and Chloramphenicol.
3. Prednisone 20 mg. t.i.d., orally.

Further tissue necrosis was halted, and by the 28th day of admission the patient was taken to the Operating Room where widespread debridement was performed. The soaks were continued. There was good wound granulation and on the 32nd day following admission, she was taken to the Operating Room again where further debridement was performed and the sloughed area were grafted, using twenty-thousandth of an inch split thickness skin graft obtained from the right thigh. A Steinmann pin was inserted through the right calcaneum and the right leg and thigh were put in traction, the grafted area being left exposed. Her postoperative course was uneventful, the graft taking well apart from small areas where minor debridement was performed. The corticosteroids were gradually decreased and stopped. The patient, much improved, was discharged home on daily saline soaks on October 20, 1969, the 70th day following admission.

Follow-up: This patient was closely followed as an outpatient, the area of injury and grafting having almost completely healed. On the 19th day following discharge (November 8, 1960), she presented with an area of cellulitis and swelling, extending above the graft and involving the right knee and lower anterior right thigh. She was immediately readmitted to the hospital. Chloromycetin therapy was instituted on the basis of previous cultures and Prednisone 20 mg. t.i.d. was recommenced. The area of cellulitis and edema rapidly subsided without necrosis. Culture of the graft area grew out Beta hemolytic Streptococcus and coagulase positive Staphylococcus. Further blood studies, including blood glucose estimations, electrophoresis and antinuclear antibody studies failed to show further abnormality. Her diabetes was at all times within control. Barium enema x-ray studies were normal. Right femoral arteriograms were performed and showed normal vessels with good lumen and filling, but there was a congenital absence of the right perineal artery. She was discharged home on the 14th day following admission on a maintenance dose of Prednisone 5 mg. b.i.d.

She has been subsequently followed on an out-patient basis with complete healing of her graft, good control of her diabetes and no recurrence of her disease. She is presently maintained on an 1800 calorie ADA diet, Diabinese 500 mg. b.i.d. and Prednisone 5 mg. daily.

Discussion

Pyoderma Gangrenosum is a rare condition, affecting females greater than males and occurring in the 30-40-year old age group mainly. It is frequently related to minor trauma with mixed Staphylococcal and Streptococcal infection. It is often associated with an underlying systemic disease.

Summary

A rare case of pyoderma gangrenosum, occurring in a fifty-one year old white female with a history of minor trauma to the right lower limb and subsequent Staphylococcal and Streptococcal wound infection. Found to be a diabetic subject with no evidence of other underlying systemic disease, but with a congenital absence of the right perineal artery in the affected limb. Successfully treated with silver nitrate soaks, corticosteroid therapy and skin grafting, but with recurrence of her disease until maintenance corticosteroid therapy was instituted.[3]

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3. Ridenhour, G. and Stephenson, H. D., Pyoderma Gangrenosum Successfully Treated with Aqueous Silver Nitrate (0.5%), Steroids and Skin Autografts, Annals of Surgery, 168: 905, November 1968.
4. Perry, H. O., et al, Malignant Pyoderma, Arches of Dermatology, 98: 561, December 1968.
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6. McCarthy, J. T., Pyoderma Gangrenosum, Medical Clinics of North America, 49-3: 764, May 1965.

141 State Street, Portland, Maine 04101

Medicare Information About Injections

In order to make accurate coverage determinations for injections, we have been advised that complete itemization is required. This itemization must include the name of the drug injected, the quantity, and the strength. These requirements apply to the process of assigned claims filed by the physician and non-assigned claims filed by the beneficiary or physician.

Many claims recently filed show the required itemization, but we consider it important to advise all physicians that payment for claims which do not contain sufficient itemization will, of necessity, be delayed. — **From Medicare Health Insurance Part B, Box 4629, Portland, Maine.**

X-Ray Of The Month*

This 53-year-old male was admitted for evaluation of fatigue, anorexia and weight loss of 15 pounds.

Retroperitoneal Fibrosis

Excessive proliferation of fibrous tissue in the retroperitoneal space was first described in 1905.[1] The varied descriptive titles indicates the wide selection of suggested etiologies. This entity has been described in association with trauma, malignancy and inflammatory disease. The suspected antecedent trauma includes previous surgical procedures and renal biopsy. Associated malignant conditions include lymphomas and adenocarcinomas of the kidney and pancreas. The inflammatory conditions one may see associated with retroperitoneal fibrosis are pyelonephritis, pancreatitis, tuberculosis of the kidney or spine, thrombophlebitis of iliac vessels, lymphopathia venereum and generalized vasculitis or arteritis. The latter has been suggested as the cause of the reversible retroperitoneal fibrosis described in patients using Sansert® (methysergide maleate).[2]

The pathologic process is a diffuse, local or segmental retroperitoneal fibrotic reaction which arises in the midline by the aortic bifurcation and extends laterally. It only rarely extends above the level of the kidneys. Two thirds of the reported cases are male, and the onset of symptoms is insidious. The most common complaint is dull flank, back or abdominal pain.

The most significant roentgen change is medial deviation of one or both ureters which may end in complete obstruction with hydronephrosis and non-function of the involved kidney. The ureteric compression in the majority of cases is at the level of the fourth and fifth lumbar vertebrae. The area of deviation and compression may be a short segment or may involve the entire ureter with the exception of its terminal part. The amount of dilatation of the urinary drainage system above the involved ureter is variable depending on the degree of compression. Angiography may reveal narrowing of the aorta and common iliac vessels.

The patient presented here had only those complaints described above. Without a histologically documented antecedent infection or underlying neoplasm, the etiology must be considered idiopathic in this case. The principal radiographic findings are demonstrated on retrograde pyelography; medial deviation and partial obstruction of both ureters at the pelvic inlet. The diagnosis was confirmed by biopsy at the time of a urinary diversion procedure (ileal loop).

*From the Department of Radiology, Maine Medical Center, Portland, Maine 04102.

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AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

Blood Test Could Provide Significant Advance in Cancer Control

NEW YORK, N. Y. — A unique international cooperative effort to verify and duplicate research findings that could lead to the long-sought simple blood test for a major form of human cancer has been initiated by the American Cancer Society and the National Cancer Institute of Canada.

The results, if confirmed, could provide a significant advance in cancer control.

Since 1965, Dr. Sam Freedman, and Dr. Phil Gold, of the Montreal General Hospital and McGill University Medical School, have been engaged in a series of experiments which showed that all human colon cancers contained identical tumor specific antigens — a substance arising from the patient's tumor, which then circulates in the blood stream. At the American Cancer Society's 1969 Science Writers' Seminar, last March, Dr. Gold reported that the antigen (called CEA, for Carcinoembryonic Antigen) disappeared from the blood of patients treated for their cancer successfully, but not from those in whom the cancer had spread.

It looked as though he had found the identifying factor in the patient's blood which would indicate if colon cancer was present, and whether, following treatment, it had all been removed.

Gold's report excited the medical community. If the CEA test proves out according to the rigid protocols of biological testing and verification, mass screening for CEA as a part of routine blood tests could be available to the general population. Medical science's goal to achieve the earliest possible detection of a major form of cancer would be realized. The ACS estimates that in 1970, 16,400 men and 18,900 women will die of cancer of the colon. (Only lung cancer kills more men; only breast cancer kills more women.)

The initial international testing effort is underway. With a grant of approximately $250,000 from the American Cancer Society to cover the United States portion of the study, together with a grant from the National Cancer Institute of Canada to cover the Canadian portion, investigators in three U. S. medical centers and two Canadian medical centers have initiated training of immunologists and technicians and a carefully designed test program.

The project's administration coordinator is Dr. A. J. Phillips, Assistant Executive Director, National Cancer Institute of Canada. He is assisted in the United States portion of the study by Dr. Sidney L. Arje, Vice President for Clinical Investigation, American Cancer Society.

The institutions involved in Canada are McGill University Medical School, Montreal, Quebec; and the University of Alberta Medical School, Edmonton. In the United States, participating institutions are the University of Michigan Medical School, Ann Arbor; Yale University Medical School, New Haven, Connecticut; and the University of Pennsylvania School of Medicine, Philadelphia.

According to Dr. Jonathan Rhoads, President of the American Cancer Society, the program is scheduled for three phases: (1) to corroborate Dr. Gold's results by double-blind studies; (2) to see if the test can be done as effectively in other laboratories as it is in Dr. Gold's lab; (3) to refine the test, and expand its application for use in judging the effectiveness of treatment.

The complete project is expected to take more than a year. Should the test prove its value it would become available for clinical use at the earliest possible time.

The procedure used in the Gold test is called a radio-immune assay. By means of this immunologic test, the antigen can be detected in a small sample of blood.

Dr. Gold is credited with the discovery of the Carcinoembryonic Antigen, and with the demonstration of circulating tumor specific antigen found in the blood of humans with cancer.

American Cancer Society News Service Release

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Ethacrynic Acid: Its Usefulness and Untoward Effects

Ethacrynic acid . . . proved to be extremely effective in treatment of various edema states. . . .

A profound diuresis may be seen in patients resistant to other diuretic agents and, in general, the properties of ethacrynic acid are similar to those in furosemide.

. . . The rapid onset of action following intravenous administration has been utilized effectively in the treatment of acute pulmonary edema. It has also been proved to be invaluable in patients with intractable heart failure and other forms of resistant edema. . . . it has been used with success in patients with chronic renal failure and acute renal failure. . . .

With increasing use . . ., numerous adverse effects have been recorded. The more serious one include agranulocytosis, acute pancreatitis, and hepatocellular damage. Other side effects include cholestatic jaundice and symptomatic hypoglycemia, and contraction of extracellular fluid volume with hypotension and collapse. Hypochloremic alkalosis, hypokalemia, and hyperuricemia may follow continued use of the drug.

An unusual side effect has been the development of acute transient deafness following intravenous use, . . . Subsequently, . . . this complication (has been reported) in five cases following oral and intravenous administration. . . .

. . . In addition, we have observed acute organic brain syndrome in two patients, probably associated with acute deafness. . . . The psychosis could be due to the superimposition of deafness in a patient with pre-existing cerebral impairment, resulting from uremia and electrolyte imbalance, or it might be the effect of acute electrolyte changes within the brain, or a combination of these factors.

The cause of the deafness following ethacrynic acid is not known. . . .

Hearing loss was unrelated to the route of administration or dosage used. There was always correlation between the onset of hearing loss and the use of ethacrynic acid. As this complication was more liable to occur in patients with renal insufficiency, we suggest that ethacrynic acid be used with caution in such patients. . . . The emergence of symptoms or changes in the audiograms are indications for withdrawal of the drug.

Submitted by Jacob B. Dana, M.D., Maine Heart Association.

Reference: Schwartz, F. D. et al, American Heart Journal, Vol. 79, pages 427-428, 1970.

Program - 117th Annual Session
Maine Medical Association

June 7, 8, 9, 1970 — The Colony, Kennebunkport

Arranged by the Scientific Committee

HAROLD D. CROSS, M.D., Hampden Highlands
Chairman

L. ARMAND GUITE, JR., M.D., Waterville

BRADLEY E. BROWNLOW, M.D., Blue Hill

Dr. Cross

Sponsors:

The Scientific Program of the annual meeting of the Maine Medical Association is made possible by the cooperation and assistance of the several organizations:

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Maine Radiological Society

Maine Chapter of the American Academy of Pediatrics

Ear, Nose and Throat Group

For this cooperation and support, the members of the Scientific Committee are grateful.

Information

Registration:

Registration throughout the session will be in the Lobby at The Colony. Registration fee $1.00.

Sunday	June 7 — 9:00 A.M. to 5:30 P.M.
Monday	June 8 — 9:00 A.M. to 6:00 P.M.
Tuesday	June 9 — 9:00 A.M. to 4:30 P.M.

Telephone: The number at The Colony is Kennebunkport, (207) 967-3331.

Visiting Delegates:

Introduction of Visiting Delegates will take place at meetings of the House of Delegates on Sunday, June 7.

Technical Exhibits:

This year twenty-three companies are contributing to the success of the annual session program by participating in the Technical Exhibits. A list of the exhibiting companies and representatives will be found on pages 100 through 101 of this program.

Sunday, June 7

9:30 A.M. First Meeting of the House of Delegates

Call to order: CHARLES R. GLASSMIRE, M.D., President-elect

Presiding: Speaker of the House, ROBINSON L. BIDWELL, M.D.

Presentation of the A. H. Robins' Physician Award for Community Service

12:30 P.M. Luncheon

3:00 P.M. Second Meeting of the House of Delegates

General Assembly (Immediately following the House of Delegates — approximately 4:30 P.M.)

Election of President-elect

6:30 P.M. Lobster Bake
Speaker: GERALD D. DORMAN, M.D., President, American Medical Association, New York, New York
Subject: To be announced

Dr. Dorman

Monday, June 8

Scientific Program

9:10 A.M. to 12:30 P.M.

Sponsored by the Maine Chapter, American Academy of General Practice.

9:10 A.M. Introductory Remarks
HAROLD D. CROSS, M.D., Hampden Highlands, Maine, Chairman, M.M.A. Scientific Committee

9:30 A.M. **Medical History Taking, Automated Techniques, Reliability**
WARNER V. SLACK, M.D., Assistant Professor of Medicine and Computer Sciences, University of Wisconsin Medical School, Madison, Wisconsin

Dr. Bjorn

Dr. Weed

10:30 A.M. **Allied Health Personnel, Their Use in Physiological Testing, Screening Procedures**
JOHN C. BJORN, M.D., Senior Attending Physician, Medical Service, Eastern Maine Medical Center, Bangor and Co-Director, PRoblem Oriented Medical Information Service, Augusta, Maine

11:00 A.M. Coffee Break

11:30 A.M. Workshops (4 groups) — **Formulation of Problem List, Plans and Follow-up**
CHARLES S. BURGER, M.D., Director, Automated Military Outpatient Service, Office of the Surgeon General of the Army, DeWitt Army Hospital, Ft. Belvoir, Virginia

JOHN C. BJORN, M.D.

LAWRENCE L. WEED, M.D., Professor of Medicine and Community Medicine, University of Vermont College of Medicine, Burlington, Vermont

HAROLD D. CROSS, M.D.

This program has been approved for 3 hours Prescribed Credit by the American Academy of General Practice Committee on Postgraduate Education.

12:30 to 2:00 P.M. Luncheon

Scientific Program

1:30 to 5:00 P.M.

Sponsored by the Maine Chapter, American College of Surgeons, the Maine Trauma Committee, and the Maine Academy of Orthopedic Surgeons.

1:30 P.M. **Business Meeting: Maine Chapter, American College of Surgeons**

2:00 P.M. **Medical Aspects of Ulcerative Colitis**
PHILIP KRAMER, M.D., University Hospital, Boston, Massachusetts

Dr. Kramer

Dr. Martin

Dr. Brownlow

Dr. Blyth

Surgical Aspects of Ulcerative Colitis
LESTER F. WILLIAMS, JR., M.D., Associate Professor of Surgery, Boston University School of Medicine and Associate Director, Third (B.U.) Surgical Service and Surgical Research Laboratory, Boston City Hospital, Boston, Massachusetts

3:00 P.M. Panel Discussion: **The Closed Reduction of Common Fractures and Their Pitfalls**
THOMAS A. MARTIN, SR., M.D., Portland, Maine, Moderator

Panelists:

Fractures of the Thumb
DALE C. BOUTON, M.D., Bangor, Maine

Fractures of the Wrist
LAWRENCE M. LEONARD, M.D., Portland, Maine

Fractures of the Elbow
PAUL STUCKI, M.D., Waterville, Maine

Fractures of the Shoulder
ANDRE P. MARCOTTE, M.D., Lewiston, Maine

6:00 to 7:00 P.M. Social Hour, Dutch Treat, Ballroom

7:00 P.M. **Annual Banquet**

Presentation of Honorary Pins

President's Address, CHARLES F. BRANCH, M.D.

Tuesday, June 9

Scientific Program

9:15 A.M. to 12:30 P.M.

Scientific speakers are supported by a grant from the Merck Sharp & Dohme Postgraduate Program.

9:15 A.M. Introductory Remarks
BRADLEY E. BROWNLOW, M.D., Blue Hill, Maine

9:30 A.M. **Use of Allied Health Personnel in the Military — AMOS Program**
CHARLES S. BURGER, M.D.

10:00 A.M. **Is the Computer Really Going to Help the Doctor?**
LAWRENCE L. WEED, M.D.

11:00 A.M. Coffee Break

11:30 A.M. Panel Discussion: **Questions and Answers Regarding Problem-Oriented Medical Record, Computers, Allied Health Personnel, Automated Techniques**

LAWRENCE L. WEED, M.D.

CHARLES S. BURGER, M.D.

JOHN C. BJORN, M.D.

BRADLEY E. BROWNLOW, M.D.

WARNER V. SLACK, M.D.

12:30 P.M. Luncheon

Scientific Program

Sponsored by the Maine Medico-Legal Society

2:00 P.M. **Gunshot and Stab Wounds**
WERNER U. SPITZ, M.D., Baltimore, Maryland

Sponsored by the Maine Medical Association's Committee on Medical Aspects of Sports.

2:00 P.M. **North Carolina High School Football Injury Study**
CARL S. BLYTH, Ph.D., Professor of Physical Education and Director, Laboratory of Applied Physiology, University of North Carolina, Chapel Hill, North Carolina

6:30 P.M. Dinner
Presentation of Golf Prizes by
DANIEL R. SHIELDS, M.D., Lewiston
Chairman, Golf Tournament

Specialty Group Meetings

Monday, June 8

2:00 to 4:00 P.M.

SECTION ON OPHTHALMOLOGY OF THE M.M.A.

KEVIN HILL, M.D., Waterville, presiding

Some Thoughts on the Diagnosis and Treatment of Retinal Disease
EPHRAIM FRIEDMAN, M.D., Professor and Chairman, Department of Ophthalmology, Boston University School of Medicine and Ophthalmologist-in-Chief, University Hospital, Boston, Massachusetts

Dr. Friedman

MAINE CHAPTER OF THE AMERICAN ACADEMY OF PEDIATRICS

MAURICE ROSS, M.D., Saco, President, presiding

Pediatric Flow Sheets and Questionnaires
JOHN C. BJORN, M.D., Senior Attending Physician, Medical Service, Eastern Maine Medical Center, Bangor and Co-Director, PRoblem Oriented Medical Information Service, Augusta, Maine

MAINE SOCIETY OF CLINICAL HYPNOSIS

JOHN P. DOW, M.D., Pittsfield, presiding

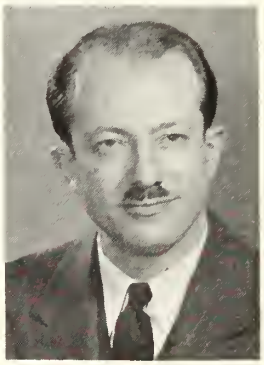
MAINE SOCIETY OF INTERNAL MEDICINE

Tuesday, June 9

10:00 A.M. — Business Meeting

MAINE MEDICO-LEGAL SOCIETY

RICHARD C. WADSWORTH, M.D., Bangor, Presiding



Dr. Mendell

Dr. Goffin

2:00 to 4:00 P.M.

MAINE RADIOLOGICAL SOCIETY

TIBOR DOBY, M.D., Portland, presiding

Arthrography of the Knee and Shoulder
PAUL J. KILLORAN, M.D., Chief of Radiology, Camden Community Hospital, Camden and Knox County General Hospital, Rockland, Maine

MAINE PSYCHIATRIC ASSOCIATION

JOHN PATTERSON, M.D., Augusta, presiding

Practice Related Aspects of the Physician's Family and Patient Families
DAVID MENDELL, M.D., Clinical Associate Professor of Psychiatry, Baylor University College of Medicine and University of Texas Graduate School of Bio-Medical Sciences, Houston, Texas

EAR, NOSE AND THROAT GROUP

Screening, Management and Analysis of Hearing Impairment in Preschool and School Children

Tumors of the Temporal Bone

FLOYD GOFFIN, M.D., Professor and Head, Division of Otolaryngology, Albany Medical Center Hospital, Albany Medical College, Albany, New York

MAINE SOCIETY OF ANESTHESIOLOGISTS

ELIO BALDINI, M.D., Portland, presiding

Obstetrical Anesthesia
JESS B. WEISS, M.D., Assistant Director, Department of Anesthesiology, Boston Lying-In Hospital, Boston, Massachusetts

Program

Woman's Auxiliary to the Maine Medical Association

Sunday, June 7

1:00-5:00 P.M. Registration

Monday, June 8

9:00 A.M.-5:00 P.M. Registration

10:00 A.M. Business Meeting
Presiding: MRS. CHARLES H. LIGHTBODY, President

12:00 NOON Social Hour

1:00 P.M. Luncheon

Greetings — CHARLES F. BRANCH, M.D., President, Maine Medical Association

Introduction of Guests

Election of Officers

Installation of Officers

Mrs. Chenault

Mrs. Lightbody

Guest Speaker — MRS. JOHN M. CHENAULT, President, Woman's Auxiliary to the AMA, Decatur, Alabama

Tuesday, June 9

A day for relaxation and visits to points of interest in the area. A list of these will be available at registration desk.

Evening Programs
See the Maine Medical Association Program on preceding pages.

Notice
Every doctor's wife is invited to attend, whether she is a member of the Auxiliary or not.

SPECIAL NOTICES

Election of a President-elect
The election of a President-elect will take place at the General Assembly, immediately following the Second Meeting of the House of Delegates, Sunday, June 7.

Election of Councilors
Election of Councilors for three years for the following Districts will take place at the Second Meeting of the House of Delegates on Sunday, June 7 at 3:00 p.m.

Fifth District — Hancock, Washington
Sixth District — Aroostook, Penobscot, Piscataquis
Third District — For one year: Knox, Lincoln-Sagadahoc to replace John F. Andrews, M.D. who has resigned.

Council Meetings
The Council will meet on Saturday, June 6 and daily throughout the session at a time and place to be announced.

Tufts Medical Alumni Reunion
Monday, June 8, 5:30 to 7:00 p.m.

Golf Tournament
Daniel R. Shields, M.D., Lewiston, Chairman

HONORARY PINS

Presentation of the Association's Honorary Pins will be made by Charles F. Branch, M.D., President of the M.M.A., at the Annual Banquet, Monday evening, June 8 at 7:00 P.M.

FIFTY-YEAR PINS

Fifty-Year Lapel Pins will be presented to the following members who were graduated from Medical School in 1920:

Cumberland County
Winifred W. Curtis, M.D., Bailey Island
Cornell University Medical College

Isaac M. Webber, M.D., Portland
Bowdoin Medical School

Dr. Curtis

Dr. Langer

Dr. Loewenstein

Kennebec County
Blynn O. Goodrich, M.D., Waterville
McGill University Faculty of Medicine

Ella Langer, M.D., Augusta
University of Vienna, Austria

Knox County
George Loewenstein, M.D., Clearwater, Florida
Friedrich-Wilhelms University, Berlin, Prussia

Oxford County
James A. MacDougall, M.D., Rumford
McGill University Faculty of Medicine

Dr. MacDougall

Dr. Woodcock

FIFTY-FIVE-YEAR PINS

Fifty-Five-Year Pins will be presented to the following members who received Fifty-Year Pins in 1965:

Cumberland County
Elton R. Blaisdell, M.D., Portland
Bowdoin Medical School

Horace K. Sowles, M.D., Falmouth
Harvard Medical School

Langdon T. Thaxter, M.D., Cumberland Foreside
Harvard Medical School

Kennebec County
Albert S. Crawford, M.D., Birmingham, Michigan
Cornell University Medical College

Penobscot County
Allan Woodcock, M.D., Bangor
Bowdoin Medical School

York County
Charles W. Kinghorn, M.D., Kittery
Bowdoin Medical School

Harold W. Stevens, M.D., Saco
Harvard Medical School

SIXTY-YEAR PIN

A Sixty-Year Pin will be presented to the following member who received his Fifty-Year Pin in 1960:

Penobscot County
Thomas A. Devan, M.D., St. Petersburg, Florida
Johns Hopkins University School of Medicine

Dr. Kinghorn

Dr. Devan

Dr. Russell

Dr. Pritham

SIXTY-FIVE-YEAR PINS

Sixty-Five-Year Pins will be presented to the following members who received Fifty-Year Pins in 1955:

Androscoggin County
Daniel F. D. Russell, M.D., Leeds
Bowdoin Medical School

Piscataquis County
Fred J. Pritham, M.D., Greenville Junction
Bowdoin Medical School

Campbell's Soups... wide variety...for limited appetites

Many people lose interest in food as they grow older. Some of them are fussy eaters—with only a few favorite foods. Others become indifferent to foods—because planning and preparing meals becomes a chore. Here Campbell's Soups can help —for these four very good reasons:

Appeal With a variety of tastes, textures, aromas, and colors, Campbell's Soups can add interest and appetite appeal. And they're easy to eat—ingredients are tender, bite-size. Even patients on special diets will find soups they can enjoy among the more than 50 different varieties available.

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Convenience Within 4 minutes a bowl of delicious soup is heated and ready to eat.

Economy Campbell's Soups are inexpensive—an important consideration to those whose budgets are limited.

Recommend Campbell's Soups . . . and, of course, enjoy them yourself. Remember, *there's a soup for almost every patient and diet . . . and for every meal.*

This is the "answering service" your patient takes home with her..

included in her Compackage™ sample of

Helpful booklet saves unnecessary phone calls—Reminds her of your directions concerning her oral contraceptive schedule . . . contains supportive instructions for "Sunday starting" . . . explains in simple language many aspects of "the pill."

Packaging helps her stay on schedule—The Ovulen Compack®, with each tablet designated by day and week of cycle, shows at a glance the last day on which a tablet was taken.

Each white Ovulen tablet contains 1 mg. ethynodiol diacetate and 0.1 mg. mestranol. Each pink tablet is a placebo, containing no active ingredients.

Ovulen-21®
Ovulen®-28
"the convenient one"

NOTE: For the budget-minded woman specify Triopak™, a three-month supply (1 Compack and 2 Refills).

Actions—Ovulen acts to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen depresses the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note: Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen is indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis and pulmonary embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration, and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable. Retrospective studies in Great Britain and the United States have shown a statistically significant association between cerebral thrombosis and embolism and the use of oral contraceptives.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen. Therefore, if such tests are abnormal in a patient taking Ovulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives.

The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

References: 1. Royal College of General Practitioners: Oral Contraception and Thrombo-Embolic Disease, J. Coll. Gen. Pract. *13*:267-279 (May) 1967. **2.** Inman, W. H. W., and Vessey, M. P.: Investigation of Deaths from Pulmonary, Coronary, and Cerebral Thrombosis and Embolism in Women of Child-Bearing Age, Brit. Med. J. *2*:193-199 (April 27) 1968. **3.** Vessey, M. P., and Doll, R.: Investigation of Relation Between Use of Oral Contraceptives and Thromboembolic Disease. A Further Report, Brit. Med. J. *2*:651:657 (June 14) 1969. **4.** Sartwell, P. E.; Masi, A. T.; Arthes, F. G.; Greene, G. R., and Smith, H. E.: Thromboembolism and Oral Contraceptives: An Epidemiologic Case-Control Study, Amer. J. Epidem. *90*:365-380 (Nov.) 1969.

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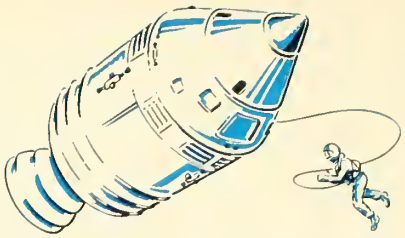

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Paul V. Davis, M.D., Bridgton
Houghton M. White, M.D., Brunswick
(1 year)
David K. Lovely, M.D., Portland
Raphael F. Turgeon, M.D., Westbrook
Kirk K. Barnes, M.D., Brunswick
Stephen E. Monaghan, M.D., Portland
John F. Gibbons, M.D., Portland
Edmund W. Hardy, M.D., Falmouth

Alternates
(2 years)
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Douglass C. Pennoyer, M.D., Portland
Domenico A. Santoro, M.D., Portland
Richard C. Dillihunt, M.D., Portland
(1 year)
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J. Paul Nadeau, M.D., Lewiston
Daniel R. Shields, M.D., Lewiston
Cyprien L. Martel, Jr., M.D., Lewiston
Ralph Zanca, M.D., Lewiston

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Alternate
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Onni C. Kangas, M.D., Rockland

Alternate
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Alternates
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Alternate
Robert C. Lecher, M.D., Belfast

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Eliot T. Stadler, M.D., West Gouldsboro

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Winston G. Stewart, M.D., Bar Harbor

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Melvin R. Aungst, M.D., Fort Kent
Harry M. Helfrich, Jr., M.D., Presque Isle
Alternates
Eugene G. Gormley, M.D., Houlton
William A. O'Brien, M.D., Presque Isle
Arthur K. Carton, M.D., Houlton

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Thornton W. Merriam, Jr., M.D., Bangor
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Stanley J. Evans, M.D., Bangor
Alternates
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Wilfred I. Butterfield, M.D., Lincoln
Russell M. Lane, M.D., Orono
John F. McGinn, M.D., Bangor
J. Robert Feeley, M.D., Bangor

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Charles H. Lightbody, M.D., Guilford
Alternate
John B. Curtis, M.D., Milo

Visiting Delegates

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BERNARD O. NEMOITIN, M.D., Stamford

The Massachusetts Medical Society

New Hampshire Medical Society
JESSE M. GALT, M.D., Dover

Medical Society of the State of New York
THOMAS F. MCCARTHY, M.D., Bronx

The Rhode Island Medical Society
HANNIBAL HAMLIN, M.D., Providence

Vermont State Medical Society
J. WARD STACKPOLE, M.D., Burlington

Delegates to Out-of-State Meetings

The Connecticut State Medical Society
FRANK W. KIBBE, M.D., Lincolnville

The Massachusetts Medical Society
STANLEY E. HERRICK, JR., M.D., Lewiston

New Hampshire and Vermont State Medical Societies
LOUIS N. FISHMAN, M.D., Lewiston

Medical Society of the State of New York
CHARLES R. GLASSMIRE, M.D., Portland

The Rhode Island Medical Society
LEONARD G. MIRAGLIUOLO, M.D., Bangor

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DEAN H. FISHER, M.D.
COMMISSIONER

State Of Maine

Department of Health and Welfare

Comprehensive Health Planning And Categorical Disease Programs*

HARRY ALLEN, M.D.**

In the July 1968 issue of the Journal, an opportunity was presented to describe the background and details of P.L. 89-749, better known as Comprehensive Health Planning. The present discussion is a follow-up to that article and deals with the relationship of the various agencies and people providing services. In New England, we are still in the process of organizing for planning, pulling gaps together, and building the relationships which will provide meaningful approaches to the problems of our health system. If there is a lesson here, it is that intervention in social processes is both uncertain and slow and requires clarity in defining objectives and the means for attaining them.

As we in the Public Health Service are all too well aware, this is a period of transition and turmoil. The Partnership of Health legislation has necessitated a reevaluation of traditional methods of rendering care at the Federal, State and local levels. Some health professionals in and out of Government are not yet committed to the process and in some discouragement has set in. The guiding principle of the planning process is that it should result in improved services to people. Here is the common meeting ground where we can explore the role of the specific disease program.

First of all, Part (a) furnishes a mandate to the State Council to gather and assess the total gamut of health-related data in order to pinpoint priority needs. Here is an opportunity for, you, the health practitioners, the researchers and the voluntary health agencies to communicate the size and scope of the diabetes or other categorical problems. It means active participation to insure the problem is an integral part of the overall plan being developed. This does not mean subplanting the original role of the voluntary health association or other agency, but rather integrating your program in the total health needs of your community. The State Health Planning Agency provides the mechanisms through which specialized planning efforts can be coordinated and related to each other. The key words are "coordinated" and "related." The concept of control would be, in my opinion, detrimental to the planning process.

The developing areawide planning agencies under Part (b) perform much the same function for a specific geographic area. This provides for a more direct input, and the participation will also insure that specific areas of high risk and identifiable populations get adequate attention. We cannot afford the luxury of duplication and competing programs for applied research and community demonstrations.

Part (d) provides block grants to the State Health and Mental Health authorities and hopefully will make more effective use of available PHS funds. It provides the needed flexibility to plan for the utilization of the funds and requires each State Program Director reevaluate existing services and develop more *impact programs* to compete for operational monies. In theory, some of these funds were to be made available for grant support for non-profit organizations. Limitations in the (d) funds have in some cases curtailed the categorical programs and, in fact, leave few dollars for distribution to other agencies.

Do you know the priority of Diabetes Programs in your State? If not, this may indicate greater need for your involvement.

Closely related to the above is the Health Service and Development Grant mechanism, Part (e), where a priority is placed on projects featuring a continuum of health services. In other words, the project must be truly *"comprehensive."* In Region I, we do not discourage good disease-oriented programs; but insist that they be "comprehensive" by supplying a missing component to total health care. In addition, priority is given to those programs directed to the poor, to inner city populations and to the medically indigent.

Continued on Page 106

*Presented at "Diabetes 1970," September 3-5, 1969, Hyannis, Massachusetts.

**Andover, Massachusetts.

Summary of Proceedings, Interim Meeting M.M.A. House of Delegates at 12:30 P.M., April 5, 1970 at Brunswick, Maine

The Interim Meeting of the Maine Medical Association House of Delegates was called to order by the President-elect, Charles R. Glassmire, M.D. and was presided over by Robinson L. Bidwell, M.D., Speaker of the House. The total attendance was 68, including 38 delegates, 13 alternates, the President, President-elect, Executive Director, 8 members of the Council, Speaker of the House, the Secretary-Treasurer and 4 guests.

Financial Statement and Proposed Budget

The financial statement for 1969 and budget proposed for 1971 was presented by Dr. Robert F. Russell, Chairman of the Budget Committee. Final action on the proposed budget will take place at the annual meeting of the House of Delegates on June 7, 1970 at The Colony, Kennebunkport, Maine.

It was recommended by several members present that the State dues be increased to $100.00 from $65.00 and that action on this take place at the June meeting.

Nominating Committee

The President-elect, Dr. Glassmire, announced the appointment of the following members to serve on the Nominating Committee:

1st District – David K. Lovely, M.D., Portland
2nd District – John R. Fenger, M.D., Norway
3rd District – George W. Bostwick, M.D., Newcastle – Chairman
4th District – George L. Temple, M.D., Belfast
5th District – Karl V. Larson, M.D., East Machias
6th District – Charles H. Lightbody, M.D., Guilford

The report of the Nominating Committee shall be the first Order of Business at the Second Meeting of the House of Delegates on Sunday, June 7 at 3:00 P.M.

Resolutions

The following resolutions were discussed and will be presented for action in June.

Somerset County –

Since the current trend in medical payments by third parties and the government, there has been a certain clerical interest in the classic history and physical examination appearing on hospital and office records; and since traditionally this information has been shared only by physicians through privileged communications, the Somerset County Medical Society wishes to reaffirm the traditional confidentiality of these records and oppose access to this information, without the patient's informed consent, by those persons or agencies not directly involved in the active care of the patient; furthermore, we strongly oppose any sanctions applied to hospital, to patients, or to physicians for failing to release this information (without patient permission). (Adopted by the Somerset County Medical Society on October 21, 1969)

Piscataquis County –

Resolved that the Maine Medical Association declare it no longer unethical for doctors of medicine to work on the same hospital staffs with qualified doctors of osteopathy. Further, that it actively encourage individual hospital staffs and boards of trustees to admit qualified osteopathic physicians to their respective staffs.

Amendments to the M.M.A. Constitution and Bylaws

Amendments to the M.M.A. Bylaws to permit acceptance to membership of qualified Doctors of Osteopathy. At the annual meeting of the House of Delegates in June 1969, it was voted to "instruct the Council to prepare the necessary amendments to the Constitution and Bylaws for acceptance of qualified doctors of osteopathy, for presentation in the manner prescribed for presentation to and action by this House at its regular annual session in 1970."

No amendments to the Constitution are necessary. Only minor amendments to the Bylaws are needed to eliminate restrictive phrases, such as "doctors of medicine" and "medical doctors."

Membership in the Maine Medical Association is contingent on membership in a component county society. At this meeting, the consensus was that the county societies should determine whether or not their respective Constitution and Bylaws would permit acceptance of qualified doctors of osteopathy, and whether or not they want to accept qualified doctors of osteopathy to membership. And, each county society to report the decision at the next meeting of the House of Delegates.

Priority Committee Reports

Reports of these committees (as listed below) were discussed at length and it was

Voted that a special meeting of the House of Delegates be held in May for further discussion of these reports, and

Voted that copies of the reports be sent to each county secretary as soon as possible. (Reports have been delivered to each county society in accordance with this directive.)

Agreed that the county societies be requested to have a county society meeting to discuss these reports before the Special Meeting of the House of Delegates in May.

Emergency Services – Euclid M. Hanbury, Jr., M.D., Chairman

Continued on Page 110

1970 — CHALLENGES AND OPPORTUNITIES

As seen by N.A.B.S.P.

As the decade of the Seventies opens, we in Blue Shield are faced with a multiplicity of challenges and opportunities.

What can be done about the rising cost of health care?

Can the health care delivery system be made more effective and equitable?

Will a national health insurance program be enacted in the Seventies and what form will it take?

In the wake of a continuation of clinical advances in medicine, what must be done in the way of providing extraordinary benefits?

These are among the key issues we face. Each is complex. Each is charged with emotions and biases.

And their interrelationship to each other creates a crisis situation.

But this crisis has not yet polarized to the point where fixed panaceas have overwhelming support. The situation is still flexible, and it is not too late to act.

What can we at Blue Shield do?

First, and we have made some strides in this direction, we must provide comprehensive benefits and make them available to those who are willing to pay for them.

Secondly, we must make the Blue Shield payment more effective and more comprehensive; we must achieve public satisfaction with our payments.

Thirdly, we must conserve the health care dollar as much as possible through adherence to our utilization review criteria.

Fourth, we must be willing to take part in experiments aimed at better health care delivery.

And finally, we must improve Plan performance in servicing our private and government programs.

While it is at the end of the list, the need to provide good service at the lowest cost and most efficiency may be our most immediate goal.

If we cannot meet this test, the entire voluntary concept of health care financing will be greatly weakened.

And if some national health care program is enacted — and the general consensus is that some form of bill will be passed in this decade — our current performance will be vital in the role the voluntary sector plays in the future.

Each of us must face the facts on performance. Each of us must be instrumental in developing programs to improve our performance. And each of us must be able to make some tough decisions to take us to the necessary level of performance.

Our future is not found by outside forces. And we must not allow ourselves to believe it is. What we do among ourselves can have tremendous impact on where this nation goes in the delivery and financing of health care.

John W. Castellucci
President
National Association of Blue Shield Plans

Associated Hospital Service of Maine

The Journal of the Maine Medical Association

DANIEL F. HANLEY, M.D., Brunswick, Editor

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Across The Desk

National Health (?) Insurance

ANOTHER NATIONAL HEALTH INSURANCE proposal now is before Congress. Sen. Jacob Javits (R-N.Y.) recently introduced a bill that would extend Medicare benefits to people of all ages by 1973. Javits said his bill, in preparation for more than a year, was drafted following consultations with New York Governor Nelson Rockefeller and former HEW Secretary Wilbur Cohen. The program would be financed by employee-employer contributions with a ceiling of 3.3% of annual wages and huge federal subsidies. The Social Security tax base would be hiked to $15,000. By 1974, the federal subsidy would be $22.7 billion, Javits said. The plan would authorize the HEW secretary to delegate administration of benefits to state agencies and to contract with existing private health insurance carriers to administer benefits regionally.

FIRST TO BE COVERED would be the disabled, unemployed and the poor. Benefits would be extended to everyone by July 1, 1973. Benefits would include dental care for children, and an annual physical checkup, including eye and ear examinations for children. Physician fees would be based on "appropriate and reasonable charges" rather than the present "reasonable charges" provided under Medicare. Javits said he realized that implementation of his program could impose a great burden on the health care system.

The Fee

FOUNDER OF KAISER-PERMANENTE plan, Sidney R. Garfield, MD, writing in *Scientific American,* has this to say about the elimination of fee-for-service in prepaid group practice: "We have come to realize that, ironically, the elimination of the fee has created a new set of problems. The obvious purpose of the fee is remuneration of the physician. It has a less obvious side effect as a potent regulator of flow into the delivery system. . . .

"ELIMINATION OF THE FEE has always been a must in our thinking, since it is a barrier to early entry into sick care . . . Only after years of costly experience did we discover that the elimination of the fee is practically as much of a barrier to early sick care as the fee itself.

"THE REASON IS that when we removed the fee, we removed the regulator of flow into the system. The result is an uncontrolled flood of well, worried-well, early-sick and sick people into our point of entry – the doctor's appointment – on a first-come, first-served basis. This overloads the system and the usurping of doctors' time by healthy people actually interferes with the care of the sick."

THE SOLUTION PROPOSED by Dr. Garfield is a new regulator "variously called multiphasic screening, health evaluation or simply health testing." National health insurance, he writes, "can only make things worse." He gives an interesting example – "Picture what would happen to, say, transportation service if fares were suddenly eliminated and travel became a right. National health insurance, if it were legislated today, would have the same effect. It would create turmoil. Even if sick care were superbly organized today, with group practice in well-integrated facilities, the change from 'fee' to 'free' would stagger the system."

In Massachusetts

A PLAN TO ESTABLISH a health care delivery system structured around neighborhood health centers has been proposed by Massachusetts Gov. Francis W. Sargent. He said the plan is aimed at halting the rise of hospital costs by making it possible for persons to be treated in their neighborhoods. Emphasis would be on preventive care. The plan calls for development of 10-15 neighborhood health centers and is designed to provide complete medical care for families.

A NON-PROFIT CORPORATION would be formed to direct provision of all types of health care

services and those providing them. Operating expenses–salaries of physicians, nurses and other providers – would be paid through Medicare, Medicaid and other third-party payors. Financing would be arranged through government grants and gifts from foundations and corporations. Legislative action may not be required to initiate the program, the governor said. The first of the health centers is scheduled to go into operation in November at Children's Hospital Medical Health Center, Boston. The chief architect of the plan is Leonard W. Cronkhite Jr., MD, general director of that center.

In Pharmacy Too

IN A POLICY REVERSAL, the American Pharmaceutical Assn. recently voted to seek repeal of state anti-substitution drug laws for which they successfully campaigned in the 1950's. The final vote was 150-89, but APhA's House of Delegates was sharply divided. Younger pharmacists generally favored the proposal, arguing that pharmacists should be more assertive in exercising their professional prerogatives and that their training and knowledge of drugs qualifies them to make decisions about filling prescriptions.

OPPOSITION FORCES argued that efforts to revise existing APhA policy would be premature for three reasons. First, they cited substantial doubt as to whether drugs made by different manufacturers really are equivalent. Second, they emphasized that anti-substitution laws do not prevent pharmacists from using hospital formulary systems or seeking physician consent to substitute a drug. They called attention to physician-pharmacist experimentation with this approach in Delaware and in some communities in other parts of the nation. Their bluntest argument, however, was that present laws prevent the possibility of pharmacists filling prescriptions with inferior products. Since 1911, AMA policy has been that no drug may be substituted without consent of the prescribing physician.

THE OUTCOME was influenced by the fact that expanding state welfare programs usually place cost limitations on drug reimbursements. If a physician prescribes a drug not listed in state formularies, or one costing more than the maximum allowed, the pharmacist has two options. He can refuse to dispense the drug or limit his charge to the amount allowable. Currently, 48 states have anti-substitution laws. Only Alaska, Missouri and the District of Columbia do not. – *From AMA Newsletter, Vol. 2, No. 16, Apr. 20, 1970*

One in Four Are Reported

A rising rate of infectious syphilis and a souring epidemic of gonorrhea "clearly out of control" demands that physicians look at an old problem with a new and stronger light.

A national survey showed that 512,906 cases of infectious VD were reported to health authorities. Actual cases were estimated to be approximately 4 times this number. These have been found for the most part in the younger age groups and, as a result, it has been recommended that routine tests for the diagnosis of gonorrhea among women should be given.

It was further recommended that the 26 states that do not have laws clearly allowing treatment of minors for VD without parental consent be urged to "review their laws and regulations in order to facilitate such treatment." (Maine Statutes do permit this.)

Corporate Practice

ONE OF RECENT PROPOSALS by *Dept. of HEW* would call on Congress to force states to dismantle all legal barriers to nonprofit group practice or *any other form of health care delivery.* This would call for elimination of prohibitions against corporate practice of medicine. Many states prohibit corporate practice of medicine. States failing to take this action by 1973 would be denied federal Medicaid funds. – *Medical News Report, Vol. 2, No. 16, Apr. 20, 1970*

DEPARTMENT OF HEALTH AND WELFARE – *Continued from Page* 102

In the needed process of reorganizing program objectives and exploring new approaches, a unique opportunity to accomplish this exists in all the major health legislation passed in the last five years. Specifically, I am referring to the entire range of disease specific programs that can and must be integrated into the Model Cities, Neighborhood Services Programs, Neighborhood Health Centers, RMP, Head Start, Medicare and Medicaid.

These programs are "major routes" through which we can influence the (1) access, (2) distribution, (3) quality, (4) financing and (5) plannning for the improvement of services to people. The role of the categorical disease program is as essential as ever and comprehensive health planning is a vital process in narrowing the gap between what is known and what is practiced. Our common goal is service. What is needed is a reevaluation of roles together with *involvement, communication* and *cooperation.*

While much time is currently being spent with the planning process, there is also a need to get on with the goal of reorganizing the major components of the health system so that the services can be provided. The problems are both challenging and imposing, but the rewards will be significant for all of us.

County Society Notes

KENNEBEC

The Kennebec County Medical Association met on February 19, 1970 at The Silent Woman Restaurant in Waterville, Maine with fifty members and guests present.

The President, George I. Gould, M.D. introduced the evening's program which was entitled "A Symposium on Continuing Medical Education." Richard T. Chamberlin, M.D. of Waterville served as Chairman and in turn introduced the other symposium members, namely, Richard P. Stetson, M.D., F.A.C.P., Boston, Massachusetts and VA Regional Liaison for Education, John R. Davy, M.D., Augusta, Joseph F. Sanders, Ph.D., Togus, and Robert L. Ohler, M.D., Togus.

Following an enjoyable and informative review of Continuing Medical Education in terms of its nationwide and local community growth, the meeting was adjourned by Dr. Gould.

FRANCIS A. SPELLMAN, M.D., *Secretary*

HANCOCK

A meeting of the Hancock County Medical Society was held on March 11, 1970 at the Blue Hill Memorial Hospital in Blue Hill, Maine with sixteen members and four guests present.

Announcements included the candidates from the County for standing and special committees of the Maine Medical Association, availability of AMA information as rebuttal to the Senate Appropriation Committee hearing on Medicare payments to physicians and Dr. Robert F. Russell's mention of the MEMPAC-AMPAC action and his recommendation for membership. The ending of the MIC program in Hancock and Washington County as of February 27th was announced. A letter from Eliot T. Stadler, M.D. to the Commissioner of Health and Welfare of the State of Maine protesting the ending of the program was read. After a discussion pro and con of the program and of the letter, a vote of 8 to 5 adopted the letter from the Society to Dr. Fisher.

The scientific portions of the program were a CPC presentation by Eji Suyama, M.D. of a death of a 36-year-old man from pulmonary embolism associated with urinary tract manipulation for stone, and a CPC discussion by Walton P. C. Clason, M.D. of the death of a 70-year-old chronic pulmonary disease victim who incidentally had an enormous coronary artery aneurysm. There followed a discussion of problems presented by these and other similar patients in our everyday practice.

BRADLEY E. BROWNLOW, M.D., *Secretary*

LINCOLN-SAGADAHOC

A meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on March 17, 1970.

The meeting was called to order by the President, Arkadij Oceretko, M.D. The minutes of the last meeting were read and accepted as read.

A letter was read from John F. Andrews, M.D. in which he resigned his position as a member of the Council of the Maine Medical Association. It was suggested that our delegates meet before the interim meeting in April to appoint a successor. George W. Bostwick, M.D. and Paul A. Fichtner, M.D. were names suggested at the meeting to fill this position.

Henry A. Hudson, M.D. then introduced Dr. Hugh Johnston, director of the endocrinology laboratory at the Maine Medical Center. Dr. Johnston presented the historical and current status of the pill. The many questions raised from the floor were evidence of the interest and timeliness of the topic.

FRANK O. AVANTAGGIO, JR., M.D., *Secretary pro tem*

Necrologies

WILLIAM V. COX, M.D.

1900-1970

William V. Cox, M.D., 69, of Auburn, Maine died on February 24, 1970. He was born in Mt. Pleasant, Ohio on August 25, 1900, son of J. Vernon and Maude M. Cox.

Dr. Cox was graduated from the University of Michigan in 1921 and received his medical degree from Harvard Medical School in 1925. He took further studies at Lakeside Hospital in Cleveland, Ohio and Peter Bent Brigham Hospital in Boston. He attended the Western Reserve Medical School and had one year of postgraduate study in Europe.

He was appointed to the surgical staff at the Central Maine General Hospital in Lewiston in 1934 and served as chief surgeon there from 1947 to 1965.

Dr. Cox was a member of the Androscoggin County Medical Association, the Maine Medical Association, the American Medical Association, the American College of Surgeons, the New England Surgical Society, the American Society of Thoracic Surgery, the Society of Military Surgeons and the Massachusetts Medical Society. He was also a diplomate of the American Board of Surgery, president of the Maine Chapter of the American College of Surgeons and was a consultant in surgery at the Veterans Administration Center in Togus, the Eastern Maine Medical Center in Bangor, the Farmington Hospital in Farmington, the Augusta General Hospital in Augusta, the Stevens Memorial Hospital in Norway and the Sanford Hospital in Sanford.

He served in both World War I and World War II. In the latter conflict, he was Lt. Colonel in the Army Medical Corps, serving in the 67th General Hospital Unit in Europe. He was awarded the Bronze Star.

Surviving are his widow, the former Dorothy Jane Thomas; one son, Dr. William V. Cox, II, of San Francisco, California; one sister, Mrs. Leonard L. McLucas of Jacksonville, Florida; two grandchildren and one niece.

Henry E. Marston, M.D.

1876-1970

Henry E. Marston, M.D., 93, of North Anson, Maine died on March 21, 1970. He was born in Waterville, Maine on August 23, 1876, son of Harry and Mary Towle Marston.

Dr. Marston was graduated from Bowdoin College in 1899 and received his medical degree from Bowdoin Medical School in 1908. He interned at the Salem City Hospital in Massachusetts for one year following his graduation from medical school.

He practiced in Pittsfield, Maine from 1909 to 1915 and then located in North Anson, Maine.

Dr. Marston was an honorary member of the Somerset County Medical Society and the Maine Medical Association, having received a 50-year pin in 1958, a 55-year pin in 1963 and a 60-year pin in 1968. He was also a member of the American Medical Association.

He is survived by his widow, the former Myrtle P. Dow of North Anson.

In Memoriam

Androscoggin County	
William V. Cox, M.D.	Auburn
Donald H. Horsman, M.D.	Auburn
Hudson R. Miller, M.D.	Auburn
Aroostook County	
Richard L. Savage, M.D.	Fort Kent
Cumberland County	
Edward G. Asherman, M.D.	Falmouth
Ernst Eppinger, M.D.	Portland
Kennebec County	
George R. Landwehr, M.D.	Augusta
Kurt A. Sommerfeld, M.D.	Gardiner
Knox County	
C. Harold Jameson, M.D.	Camden
Penobscot County	
Forrest B. Ames, M.D.	Brewer
John E. Burke, M.D.	Bangor
Wesley C. McNamara, M.D.	Lincoln
Magnus F. Ridlon, M.D.	Bangor
Piscataquis County	
Albert M. Carde, M.D.	Milo
Somerset County	
William B. Grow, M.D.	China
Henry E. Marston, M.D.	North Anson
Tadeo Zbyszycki, M.D.	Skowhegan
York County	
Carl G. Dennett, M.D.	Saco
Joseph R. Larochelle, M.D.	Biddeford

News, Notes and Announcements

Stoma Clinic

Maine's first stoma rehabilitation clinic opened at Maine Medical Center, April 16, 1970, to meet the physical, educational and emotional needs of the person with a problem related to a stoma (colostomy, ileostomy or ileal conduit).

To be scheduled monthly, the new clinic will be staffed by physicians and nurses with special interest in stoma care, and a nurse enterostomal therapist with preparation and experience in meeting the needs of a person with an ostomy.

It is assumed that self care is taught in the hospital where the surgery is performed, but if the patient continues to have a problem with the appliance, the skin or irrigations, this clinic is designed to be a resource where the patient may receive further instruction, encouragement and assistance in living with his ostomy. It is not to be a follow-up medical-surgical clinic.

Patients should be referred by their own physicians, but the clinic is open to any person with a stoma. Referring physicians will receive a consultation report with recommendations.

Appointments will be required and may be made by writing or telephoning the Stoma Clinic, Maine Medical Center, 871-2676.

Medical information should be provided to the Stoma Clinic prior to the visit. Patient charges will cover a professional fee and hospital services. Adjustments may be made when necessary.

State of Maine Board of Registration of Medicine Secretary — George E. Sullivan, M.D. Waterville, Maine

Physicians Licensed to Practice Medicine and Surgery in the State of Maine — 1969-1970

Through Examination

Silverio Agujar, Jr., M.D., Columbia St., West Union, W. Va.
Vivian M. J. Barretto, M.D., Salem Hosp., Salem, Mass.
Eashwara Bhoothalingam, M.D., Taunton State Hosp., Taunton, Mass.
Vlastimil Capek, M.D., 344 S. Maple Ave., Oak Park, Ill.
Sosthene Casthely, M.D., 1770 Grand Concourse, Bronx, N.Y.
Pierre Darbouze, M.D., Queens Hosp. Ctr., Jamaica, N.Y.
Naresh K. Dua, M.D., 80-15-41 Ave., Elmhurst, N.Y.
Mario N. N. Gomes, M.D., 1931 N. Cleveland St., Arlington, Va.
John F. Griffin, M.D., 6 Univ. Rd., Harvard Sq., Cambridge, Mass.
Hernan L. Guiang, M.D., 1701 Gardenia Ave., Royal Oak, Mich.
Saeed Hakim, M.D., 104-60 Apt. IV, Queens Blvd., Forest Hills, N.Y.
Aladar Kabok, M.D., 1325 South Grand, St. Louis, Mo.
Francis Kleyna, M.D., 37 Deering St., Portland, Me.
Martin Laster, M.D., 45 Hospital Rd., Harding, Mass.
Raghunath M. Mehta, M.D., Taunton State Hosp., Taunton, Mass.
Marcus W. Melvin, M.D., 750 Harrison Ave., Boston, Mass.
Igor Mihajlov, M.D., 2146 Broadway St., Toledo, Ohio
Gholamali Mozaffarian, M.D., Maine Medical Ctr., Portland, Me.
Mohammad Nasrullah, M.D., Medfield State Hosp., Harding, Mass.
Bedi S. Okay, M.D., Seton Hospital, Waterville, Me.
Satya P. Sahukar, M.D., 2072-20th Lane, Brooklyn, N.Y.
Jan S. Scheffs, M.D., 2510 Ocean Parkway, Brooklyn, N.Y.
Shamim A. Shamsi, M.D., 2 Autumn St., Boston, Mass.
Behzat Sivisoglu, M.D., 591 Morton St., Boston, Mass.
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Two Maine Specialists Admitted To American College of Cardiology

Two Maine doctors have been granted Fellowships in the American College of Cardiology (ACC), the national medical society for specialists in cardiovascular diseases. The doctors are among a group of 167 from the United States, Canada, and Mexico recently admitted to the College's highest membership classification.

Wilbur B. Manter, M.D., Bangor, Maine, the ACC Governor for Maine, listed the new Fellows as *Paul R. Minton, M.D., Portland and Harold L. Osher, M.D., Portland.*

The two doctors, as well as the other new Fellows, have fulfilled stringent membership requirements based on several years of practice and specialty certification. This effort, according to Dr. Manter, culminates in their being considered by colleagues in their communities as specialists or consultants in cardiovascular diseases.

SUMMARY OF PROCEEDINGS, INTERIM MEETING M.M.A. HOUSE OF DELEGATES
Continued from Page 103

Ethics and Discipline – Robert O. Kellogg, M.D., Chairman
Health Manpower and Recruitment – Ferris S. Ray, M.D., Chairman
Comprehensive Health Planning – Robert P. Andrews, M.D., Chairman
Medicine and the Law including Malpractice – John P. Dow, M.D., Chairman
Nursing Needs – George O. Chase, M.D., Chairman
Osteopathy – George W. Bostwick, M.D., Chairman
Paramedical Personnel – George W. Hallett, M.D., Chairman
Peer Review – Harold D. Cross, M.D., Chairman
Organization – George F. Sager, M.D., Chairman
Distribution of Health Services – John C. Van Pelt, M.D., Chairman
Health Financing – Thornton W. Merriam, Jr., M.D., Chairman

Committee Reports

Reports were presented by the following committees:
*Liaison Activities Between the Maine State Nurses Association and the Maine Medical Association – William L. MacVane, Jr., M.D., Chairman
*Liaison Committee Between the Maine State Bar Association and the Maine Medical Association – John A. Woodcock, M.D., Chairman
*Diabetes – Melvin Bacon, M.D., Chairman
*School Health – Marion K. Moulton, M.D., Chairman
Scientific Committee – outline of Annual Session Program – Harold D. Cross, M.D., Chairman

Discussion concerning *ambulance driver's license* was opened by Dr. John P. Dow, who was instructed to bring in a report in June of what he wants done relative to this matter.

Election of Councilors

The members were reminded that election of Councilors for the following Districts will take place at the Second Meeting of the House of Delegates on Sunday, June 7 at 3:00 P.M.

Fifth District (Hancock, Washington)
Sixth District (Aroostook, Penobscot, Piscataquis)
Third District (Knox, Lincoln-Sagadahoc) for one year to replace John F. Andrews, M.D. who has resigned.

It was announced that a $2,000.00 grant to the Maine Medical Education Foundation has been received from the American Cancer Society, Maine Division, Inc. This presentation was made at the meeting of the Council which preceded the Interim Meeting of the House of Delegates.

Charles F. Branch, M.D., President of the M.M.A. receives a grant for the M.M.E.F. from the American Cancer Society, Maine Division, Inc. Presentation of the grant is made by Mrs. Esther M. Kennard, Volunteer Secretary of the Maine Division.

Adjournment at 5:30 P.M.

*Reports of these committees have been sent to the President and Secretary of each County Society and to all delegates and alternates. Action on these reports, where indicated, will take place in June.

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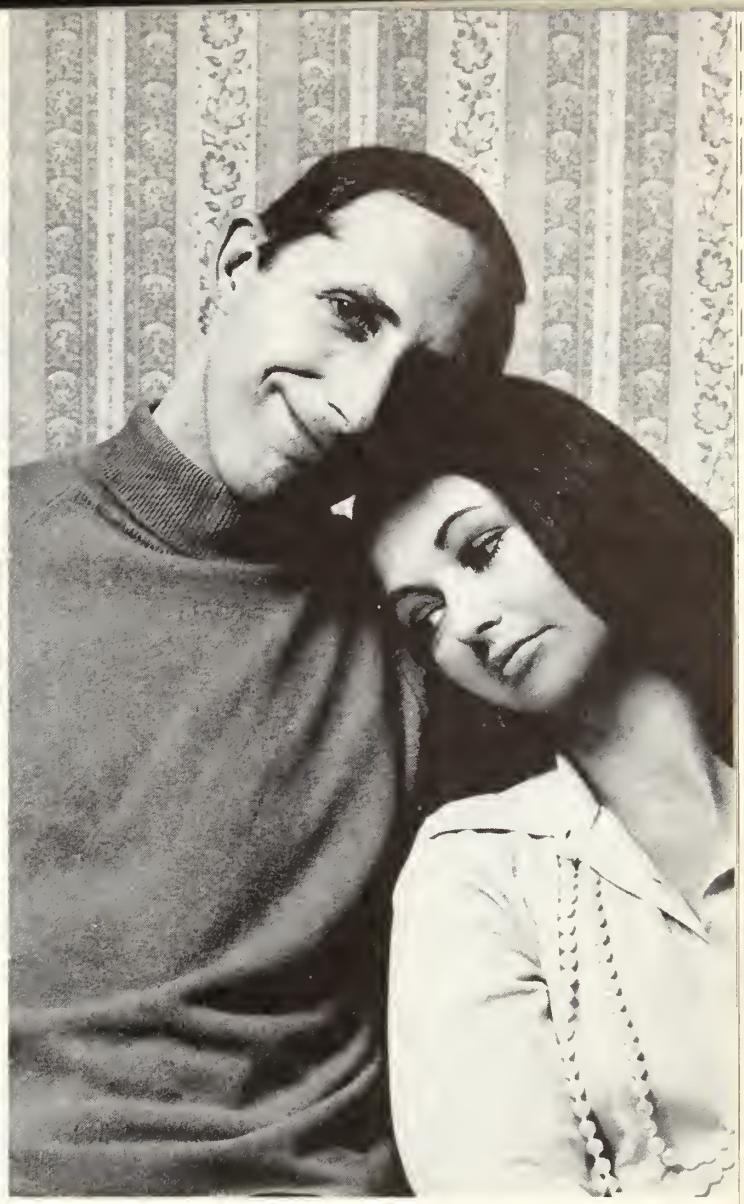

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.*: Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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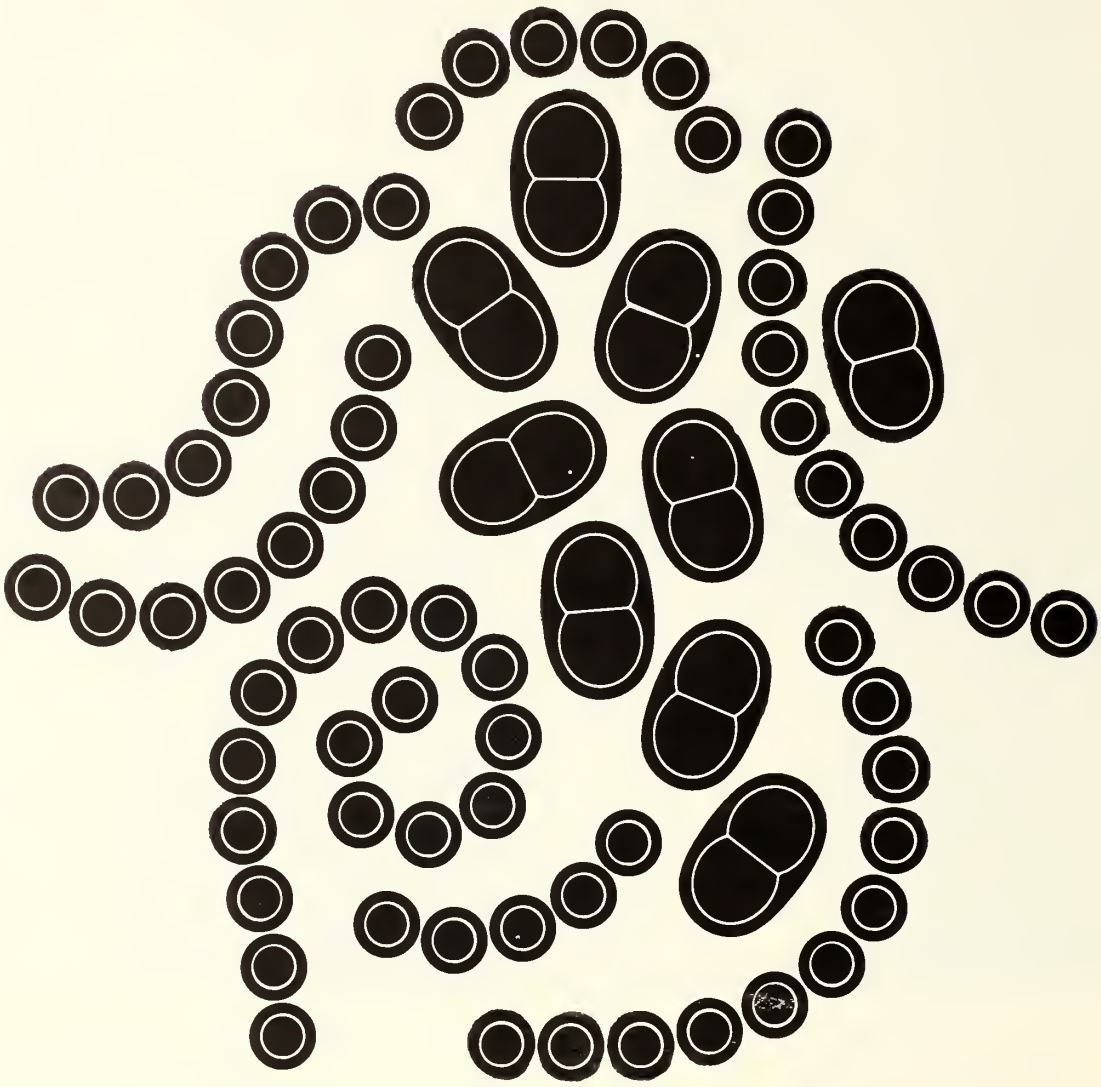

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Warning: Not intended for treatment of pernicious anemia or other primary or secondary anemias. Neurologic involvement may develop or progress, despite temporary remission of anemia, in patients with pernicious anemia who receive more than 0.1 mg of folic acid per day and who are inadequately treated with vitamin B_{12}.

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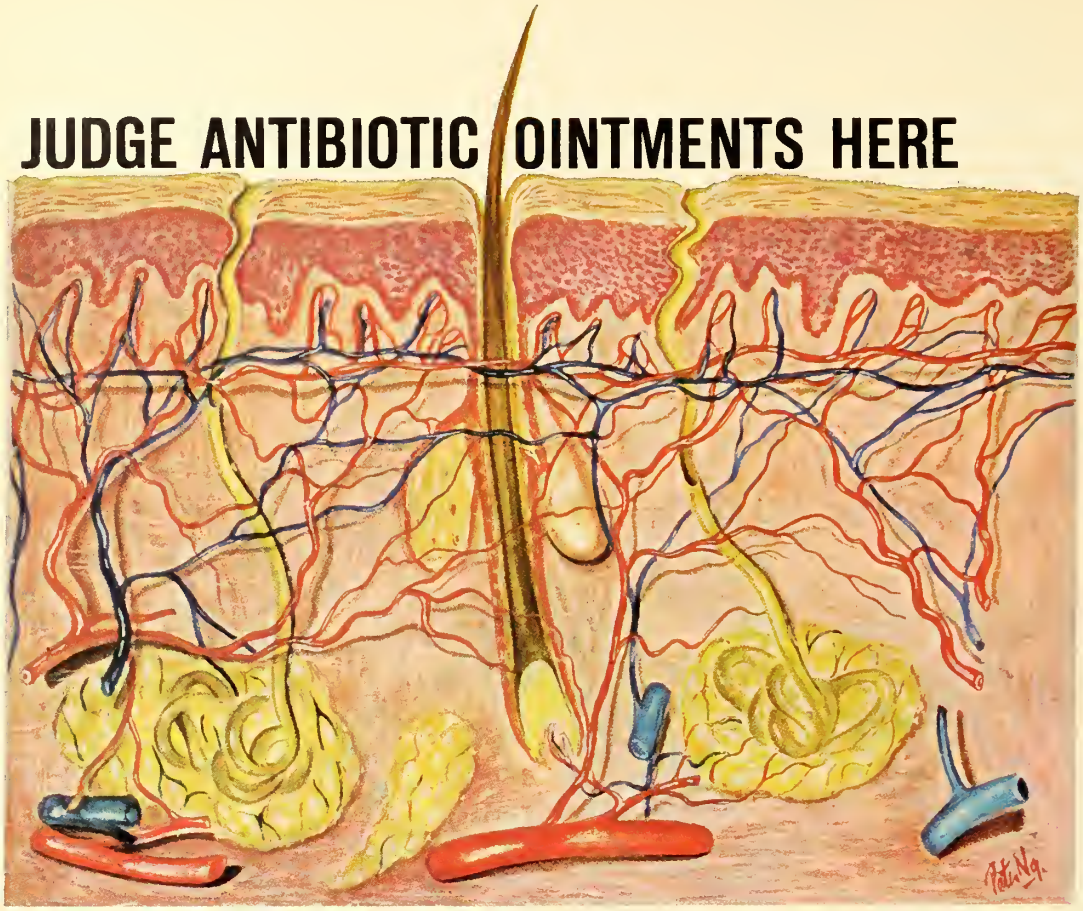

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Supplied: Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.

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you are considering weight reduction, consider

Preludin®

phenmetrazine hydrochloride
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prolonged-action tablets

Often effective

Controlled studies in a general patient population have shown that when Preludin is used with diet, the rate of weight loss exceeds that obtained by placebo and diet.

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Slow, even release of the active principle usually suppresses appetite continuously for about 12 hours.

Once-a-day dosage

One Endurets tablet after breakfast. It helps reduce weight and costs, conveniently.

For contraindications, warning, precautions, and adverse reactions, please see the full prescribing information.
It is summarized on this page.

Where there's no will there's a therapeutic way.

*Among persons 20% or more overweight as compared with median weight for persons of like height and sex.

1. Kannel, W.B., *et al.*: *Circulation* 35:734, 1967.
2. Thomas, H.E., Jr., *et al.*: *Med. Times* 95:1099, 1967.
3. Albrink, M.J., in: Beeson, P.B. & McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Phila.: W.B. Saunders Co., 1967.

Preludin®
phenmetrazine hydrochloride

Preludin is indicated only as an anorexigenic agent in the treatment of obesity. It may be used in simple obesity and in obesity complicated by diabetes, moderate hypertension (see Precautions), or pregnancy (see Warning).

Contraindications: Severe coronary artery disease, hyperthyroidism, severe hypertension, nervous instability, and agitated prepsychotic states. Do not use with other CNS stimulants, including MAO inhibitors.

Warning: Do not use during the first trimester of pregnancy unless potential benefits outweigh possible risks. There have been clinical reports of congenital malformation, but causal relationship has not been proved. Animal teratogenic studies have been inconclusive.

Precautions: Use with caution in moderate hypertension and cardiac decompensation. Cases involving abuse of or dependence on phenmetrazine hydrochloride have been reported. In general, these cases were characterized by excessive consumption of the drug for its central stimulant effect, and have resulted in a psychotic illness manifested by restlessness, mood or behavior changes, hallucinations or delusions. Do not exceed recommended dosage.

Adverse Reactions: Dryness or unpleasant taste in the mouth, urticaria, overstimulation, insomnia, urinary frequency or nocturia, dizziness, nausea, or headache.

Dosage: One 25 mg. tablet b.i.d. or t.i.d. Or one 75 mg. Endurets tablet a day, taken by mid-morning.

Availability: Pink, square, scored tablets of 25 mg. for b.i.d. or t.i.d. administration, in bottles of 100 and 1000.
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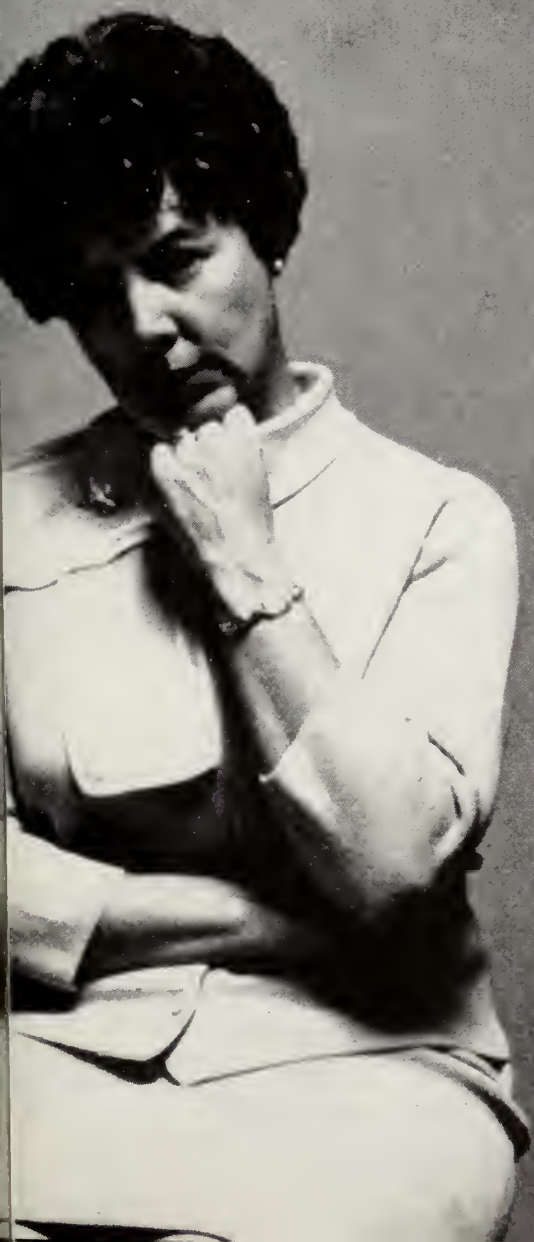

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(INDOMETHACIN | MSD)

helps relieve pain, fever, swelling, and tenderness

Please see new prescribing information on following page.

REVISED PRESCRIBING INFORMATION

IMPORTANT NOTE: INDOCIN (Indomethacin, MSD) cannot be considered a simple analgesic and should not be used in conditions other than those recommended under Indications. The drug should not be prescribed for children because safe conditions for use have not been established.

General Adverse Effects: Because of the high potency of the drug and the variability of its potential to cause adverse reactions, the following are strongly recommended: 1) the lowest possible effective dose for the individual patient should be prescribed. Increased dosage tends to increase adverse effects, particularly in doses over 150-200 mg/day, without corresponding clinical benefits; and 2) careful instructions to, and observations of, the individual patients are essential to the prevention of serious and irreversible, including fatal, adverse reactions, especially in the aging patient.

Indications: Symptomatic relief of adult rheumatoid and degenerative joint disease unresponsive to adequate trial of salicylates and other measures of established value, such as appropriate rest. Has been found effective in active stages of: 1) moderate to severe rheumatoid arthritis including acute flares of chronic disease, 2) moderate to severe rheumatoid (ankylosing) spondylitis, and 3) moderate to severe degenerative joint disease of the hip (osteoarthritis of the hip). Has been found effective in relieving pain and reducing fever, swelling, and tenderness in acute gouty arthritis in selected patients. May enable reduction of steroid dosage in patients receiving steroids for the more severe forms of rheumatoid arthritis; in such instances the steroid dosage should be reduced slowly and the patients followed very closely for any possible adverse effects.

Contraindications: Children 14 years of age and under; pregnant women and nursing mothers; active gastrointestinal lesions or history of recurrent gastrointestinal lesions; allergy to aspirin and indomethacin.

Warnings: *Gastrointestinal Effects:* Because of the occurrence and, at times, severity of gastrointestinal reactions, be continuously alert for any sign or symptom signaling a possible gastrointestinal reaction. The risks of continuing therapy with INDOCIN in the face of such symptoms must be weighed against the possible benefits to the individual patient. Gastrointestinal effects may be reduced by giving the drug immediately after meals, with food, or with antacids. Use greater care in aging patients.
Ocular Effects: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients on prolonged therapy. Discontinue therapy if such changes are observed. Ophthalmologic examination at periodic intervals is desirable in patients on prolonged therapy.
Central Nervous System Effects: INDOCIN (Indomethacin, MSD) may aggravate psychiatric disturbances, epilepsy, and parkinsonism, and should be used with considerable caution in patients with these conditions. If severe CNS reactions develop, discontinue the drug.

Precautions: Blurred vision may be a significant symptom that warrants a thorough ophthalmologic examination. Patients should be cautioned about engaging in activities requiring mental alertness and motor coordination, as driving a car. Headache which persists despite dosage reduction requires complete cessation of the drug. May mask the usual signs and symptoms of infection; therefore, the physician must be continually on the alert for this and should use the drug with extra care in the presence of existing controlled infection. After the acute phase of the disease is under control, an attempt to reduce the daily dose should be made repeatedly until the patient is off entirely.

Adverse Reactions: *Gastrointestinal Reactions:* Single or multiple ulcerations of the esophagus, stomach, duodenum, or small intestine, including perforation and hemorrhage, with fatalities in some instances; gastrointestinal bleeding without obvious ulcer formation; perforation o preexisting sigmoid lesions (diverticulum, carci noma, etc.); rarely, increased abdominal pain i ulcerative colitis patients or development of ul cerative colitis and regional ileitis; gastritis which may persist after the cessation of th drug; nausea, vomiting, anorexia, epigastric dis tress, abdominal pain, and diarrhea.
Eye Reactions: Corneal deposits and retinal dis turbances, including those of the macula, hav been observed on prolonged therapy; blurring o vision.
Hepatic Reactions: Rarely, toxic hepatitis an jaundice, including some fatal cases.
Hematologic Reactions: Aplastic anemia, hemo lytic anemia, bone marrow depression, agranulo cytosis, leukopenia, and thrombocytopenic pur pura. Since some patients manifest anemia sec ondary to obvious or occult gastrointestina bleeding, appropriate blood determinations ar recommended.
Hypersensitivity Reactions: Acute respiratory dis tress, including dyspnea and asthma; angiitis pruritus; urticaria; angioedema; skin rashes.
Ear Reactions: Hearing disturbances, deafness tinnitus.
Central Nervous System Reactions: Psychotic ep sodes, depersonalization, depression, coma, cor vulsions, peripheral neuropathy, drowsiness mental confusion, lightheadedness, dizziness headache.
Cardiovascular-Renal Reactions: Edema, elevatio of blood pressure, hematuria.
Dermatologic Reactions: Loss of hair, erythem nodosum.
Miscellaneous: Rarely, vaginal bleeding, hyper glycemia, glycosuria, ulcerative stomatitis, an epistaxis.

Supplied: Capsules containing 25 mg indometh acin each, in bottles of 100 and 1000; capsule containing 50 mg indomethacin each, in bottle of 100.

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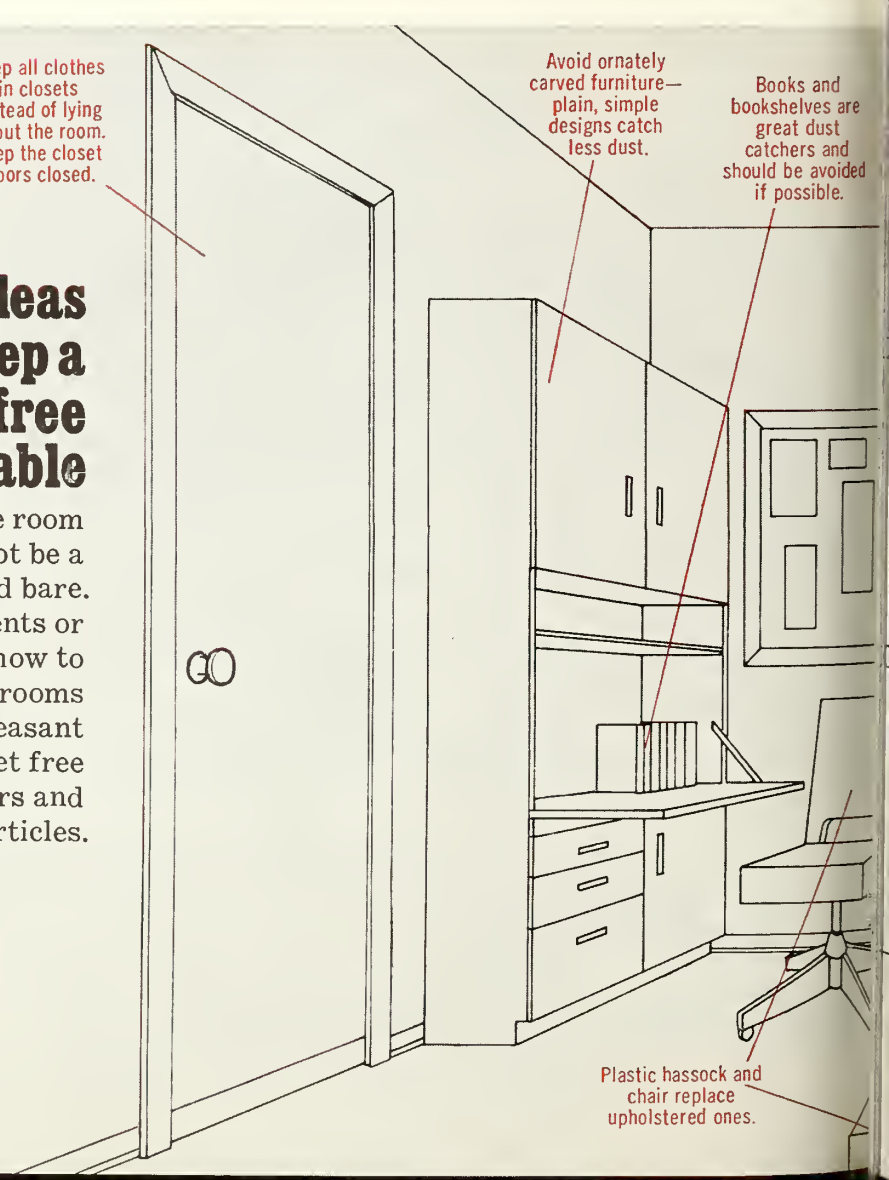

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CAUTIONS: Until response is determined, patient should be oned against engaging in mechanical operations requiring iess.

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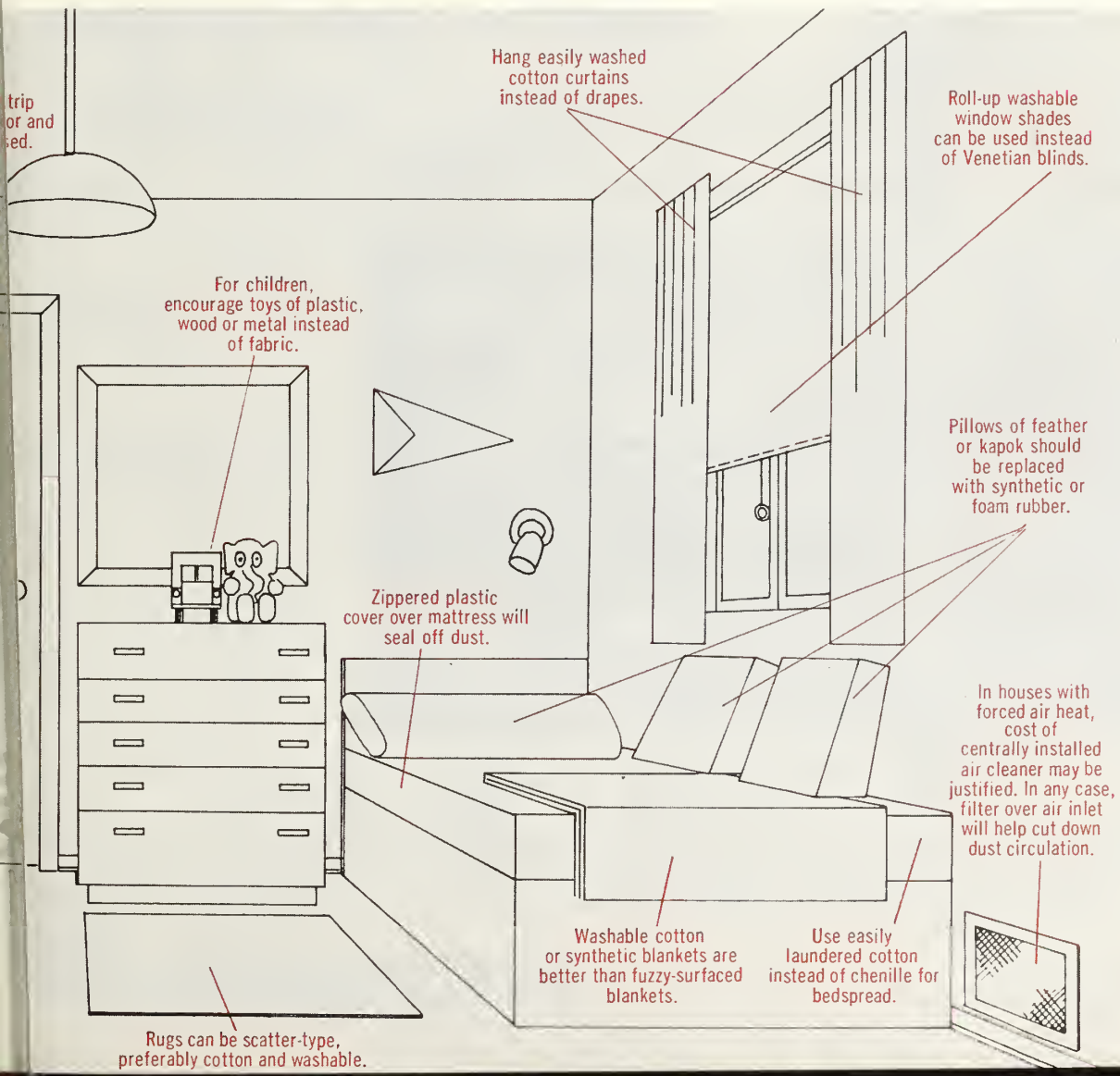

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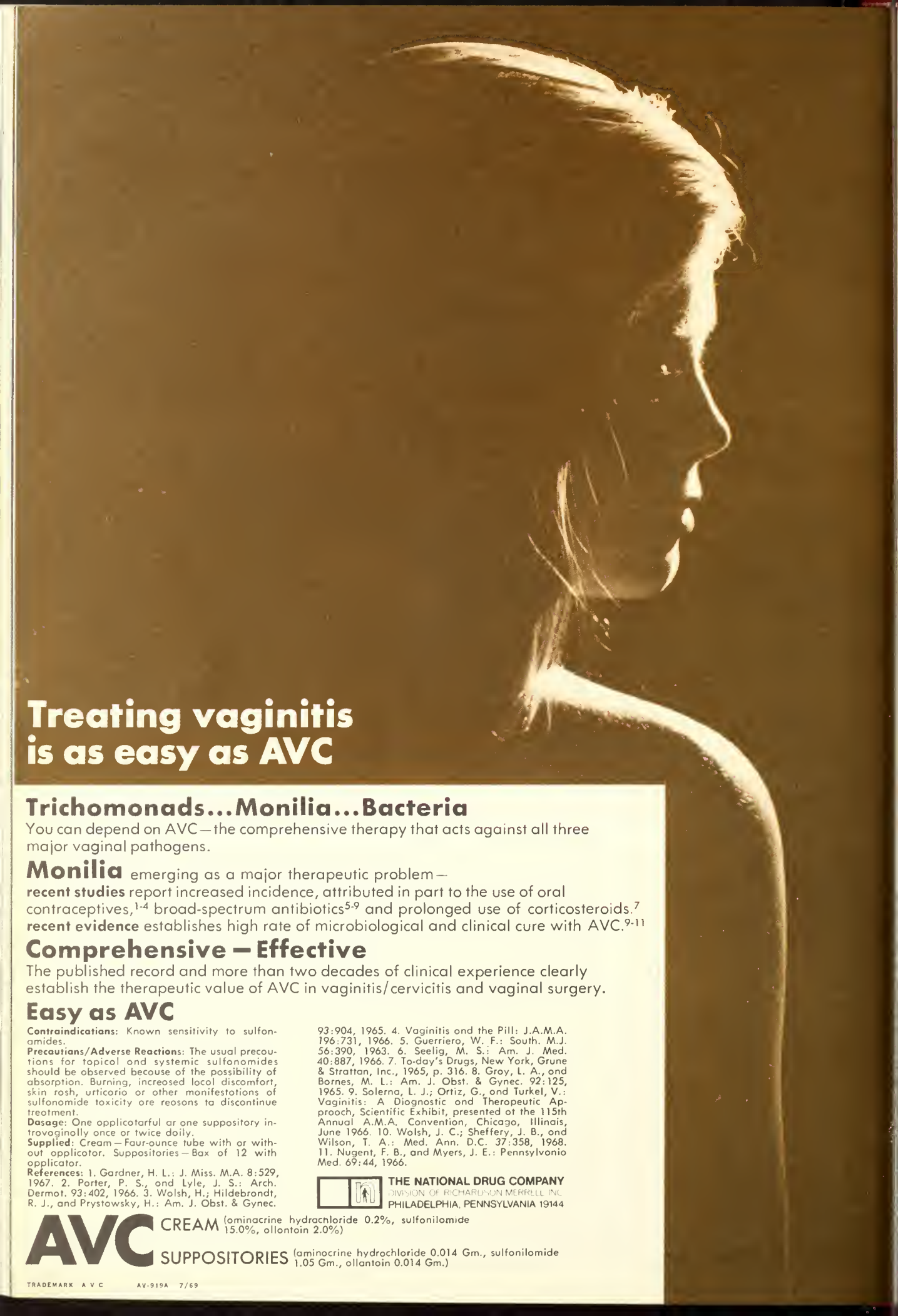

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References: 1. Gardner, H. L.: J. Miss. M.A. 8:529, 1967. 2. Porter, P. S., and Lyle, J. S.: Arch. Dermat. 93:402, 1966. 3. Walsh, H.; Hildebrandt, R. J., and Prystowsky, H.: Am. J. Obst. & Gynec. 93:904, 1965. 4. Vaginitis and the Pill: J.A.M.A. 196:731, 1966. 5. Guerriero, W. F.: South. M.J. 56:390, 1963. 6. Seelig, M. S.: Am. J. Med. 40:887, 1966. 7. To-day's Drugs, New York, Grune & Strattan, Inc., 1965, p. 316. 8. Gray, L. A., and Barnes, M. L.: Am. J. Obst. & Gynec. 92:125, 1965. 9. Solerna, L. J.; Ortiz, G., and Turkel, V.: Vaginitis: A Diagnostic and Therapeutic Approach, Scientific Exhibit, presented at the 115th Annual A.M.A. Convention, Chicago, Illinois, June 1966. 10. Walsh, J. C.; Sheffery, J. B., and Wilson, T. A.: Med. Ann. D.C. 37:358, 1968. 11. Nugent, F. B., and Myers, J. E.: Pennsylvania Med. 69:44, 1966.

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Precautions: Nonsusceptible organisms may overgrow; treat superinfection appropriately. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).
Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage. Upon adverse reaction, stop medication and treat appropriately.

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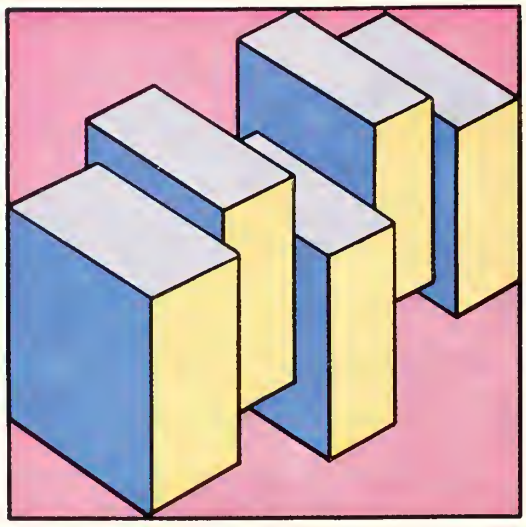

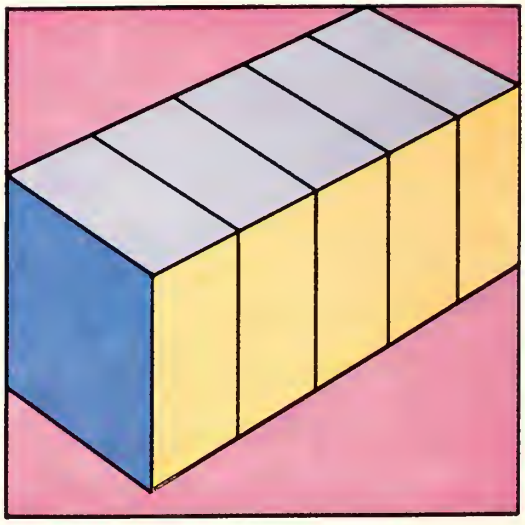

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INDICATIONS: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.
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PRECAUTIONS: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.
ADVERSE REACTIONS: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido--all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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(1) Siver, R. H.: CMD, *21*:109, September 1954. (2) Frykman, H. H.: Minn. Med., *38*:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., *51*:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., *15*:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., *58*:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, *25*:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., *20*:591-593, November 1965.

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* ESTHER M. KENNARD, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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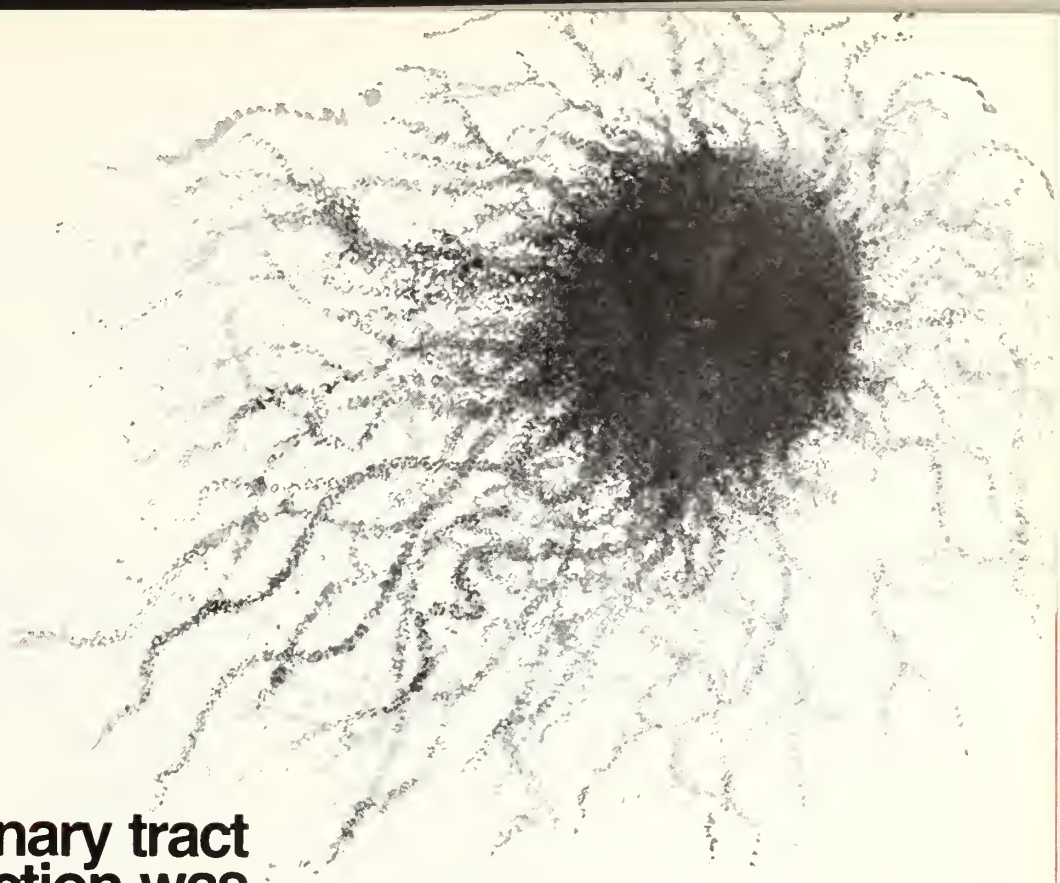

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Precautions: Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects: Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose-related. Transient, reversible, nephrogenic diabetes insipidus with excessive thirst and polyuria (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth—dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy. Demethylchlortetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.

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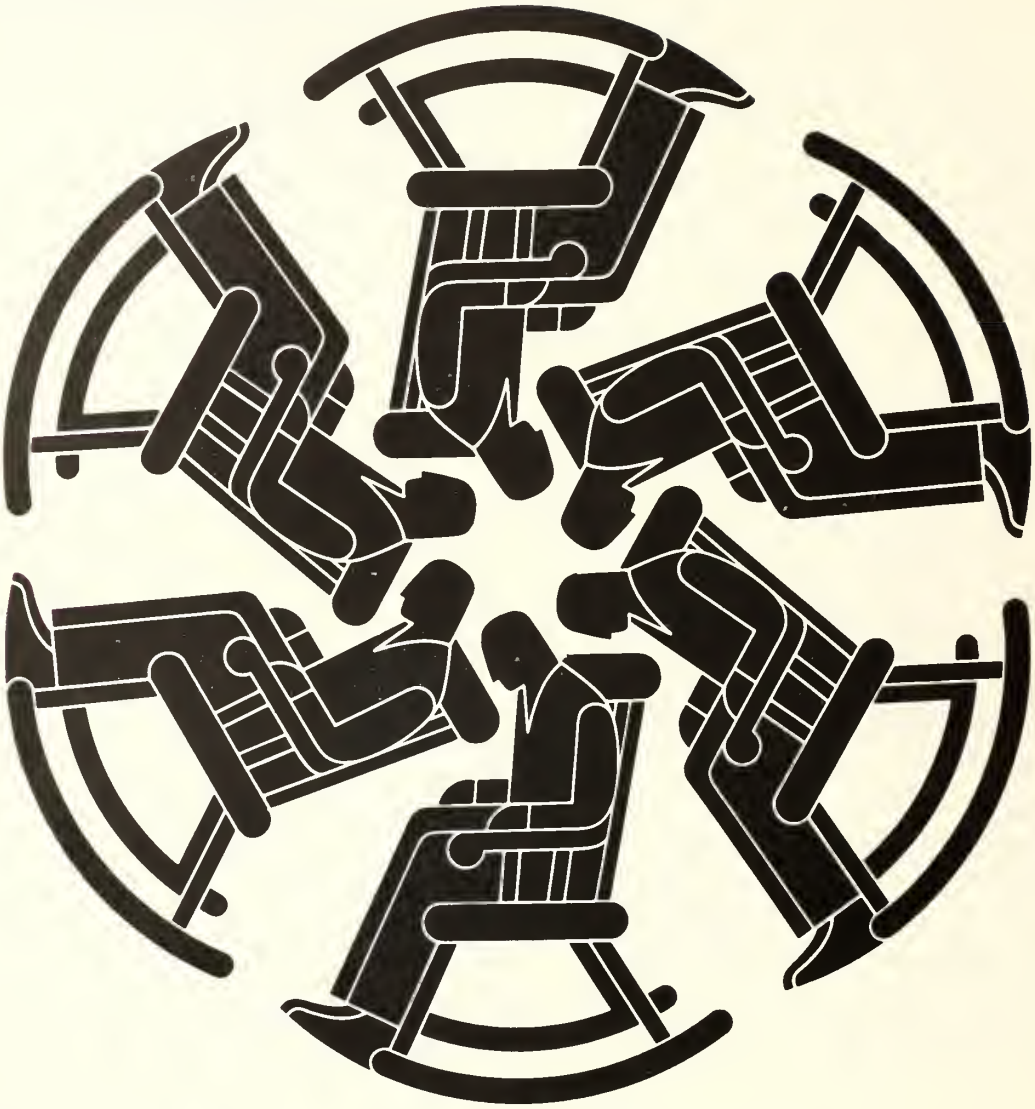

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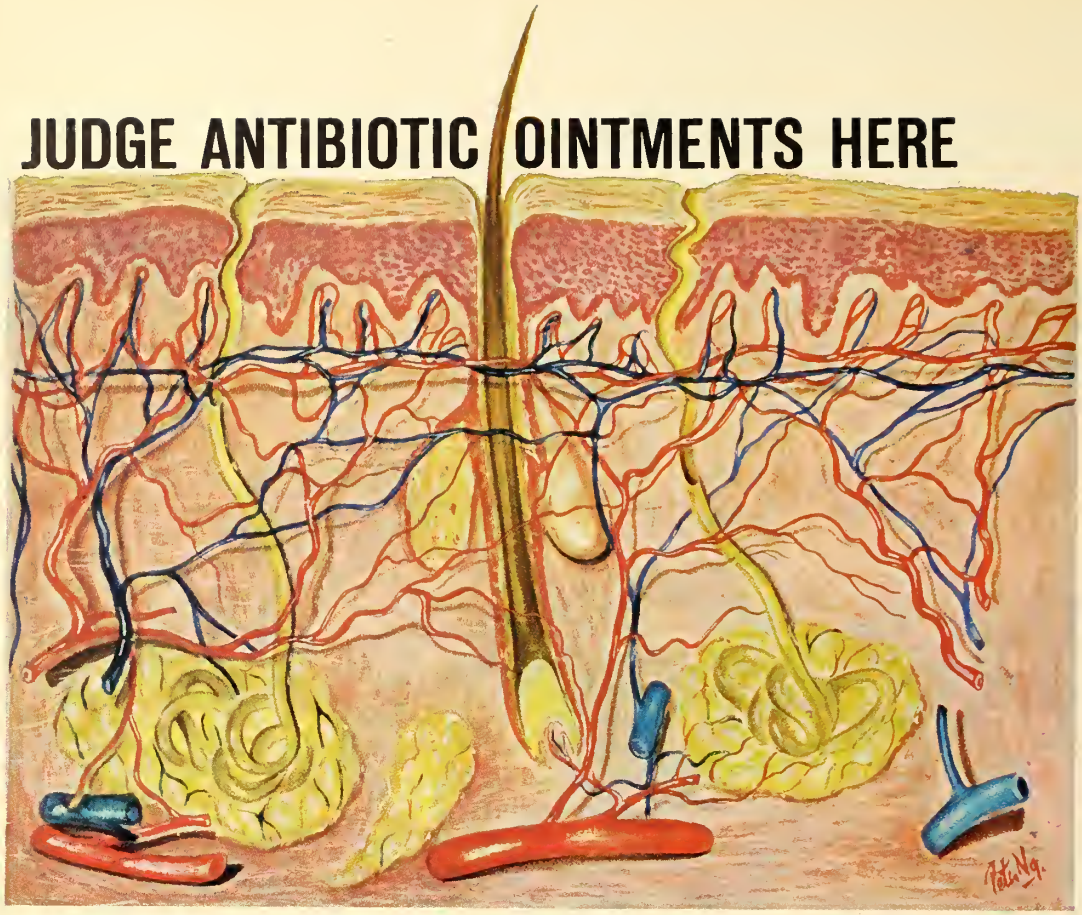

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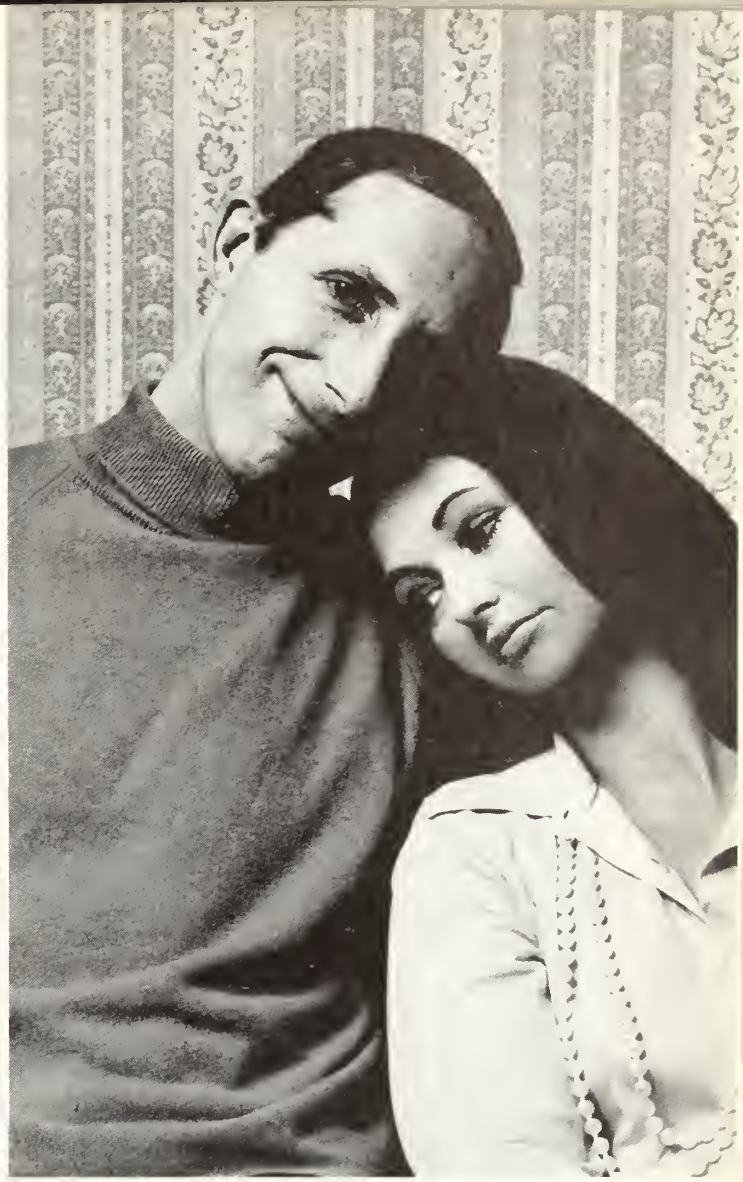

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.*: Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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The Journal of the Maine Medical Association

Volume Sixty-one | Brunswick, Maine, June 1970 | Number 6

Patient Origin Study

An Analysis of Data on Maine Towns, Populations, Hospitals and Admissions

JEFFERSON ACKOR and DAVID SOULE

A report entitled *Patient Origin Study: An Analysis of Data on Maine Towns, Populations, Hospitals and Admissions* recently completed by the Health Facilities Planning Council describes the results of a study of all admissions to Maine acute care hospitals for the calendar year 1968.

The report's findings can be grouped into four significant areas:

Definition of service areas and service population for Maine hospitals;

Patterns of movement of hospital patients between service areas;

Rates of admissions per thousand population for each Maine hospital community;

General observations on Maine hospitals and communities.

The report's conclusions are derived from statistical data generated from a one hundred percent sample of hospital admissions specifying the town of residence of all patients admitted during the year 1968. No information other than town of residence was obtained.

The decision to concentrate on residence data only was based upon two considerations. First, it was felt that the responses from the hospitals were more likely to be prompt and complete if the data requested were kept to a minimum. Second, with only the one category of information as a beginning, the data would be much more readily manageable. More extensive data could be incorporated into later studies.

There were two major reasons for obtaining information on a 100% sample. First, many of the hospitals and towns in Maine are so small that obtaining data on any less than a 100% basis could be inaccurate for them. This type of inaccuracy could have affected hospital community delineation, determination of population served, and admission rates.

The other reason was the precedent-setting nature of this study. Since considerable future research is expected to be based on the results of the *Patient Origin Study,* it was felt that the accuracy of the study should be above reproach. Thus, a complete sample was indicated.

The original source information, as it was received from each hospital, consisted simply of a list of all the towns whose residents had been admitted to the hospital in 1968, together with the number of admissions from each town.

Because the analysis and tabulation of the data would involve handling a large number of separate data elements, the Council made maximum use of systems analysis techniques and data processing methods. A data processing system for the *Patient Origin Study* was set up, programmed, and ready to use by the time the last of the patient origin data had been received from the hospitals.

The report lists the result of this collection and processing effort in several ways. Hospital service areas, called "hospital communities," are defined. The towns composing each hospital community are specified, and their populations are calculated. The hospital admission rates are calculated for the population of each hospital community. Patterns of patient movement between hospital communities are described. The specific populations served by each of Maine's hospitals is calculated. The composition of each hospital's admissions is broken down and analyzed according to the original residence of the patients.

Throughout the report, the presentation of data is accompanied by analysis and interpretation of the data.

Conclusions and general observations are spaced throughout the discussion of each of the various aspects of hospital use. Finally, the report concludes with individualized summaries of data for each of the 45 hospital communities in the State of Maine.

Definition of Hospital Service Areas

There are 60 voluntary acute care general hospitals in Maine. The HFPC report has defined 45 hospital communities served by these hospitals. (Some hospital communities are served by more than one hospital.)

The Council defines a hospital community as a group of towns which are served by a single hospital or by several hospitals. The hospital communities are so defined that the hospital or hospitals in each one serve a clear majority of the community's residents – usually two-thirds or more. The hospital community is the base on which most of the statistics in the *Patient Origin Report* are tabulated.

In addition to being broken down by individual towns and hospital communities, the data are arranged and tabulated by the five health planning regions within the State of Maine. These regions are combinations of hospital communities which were originally established following a 1964 Patient Origin Report based on a five-week sample of hospital admissions.

The five regions are those which now serve as a basis for regional comprehensive health planning in Maine. The regions and their central locations are as follows: Southern Maine Region, Portland; Tri-County Region, Lewiston; Upper Kennebec Valley Region, Waterville; Penobscot Valley Region, Bangor; and Aroostook Region, Central Aroostook County.

The regions are determined as the last step in a progressive process. The hospital communities are defined as groups of towns, and then the regions are defined as groups of hospital communities.

Following the definition of hospital communities and regions, the report provides total populations for each community and region. The populations provided are based on 1970 estimates made by the Public Affairs Research Center of Bowdoin College, Brunswick, Maine.

Population Served by Maine Hospitals

The report notes that there are 60 short-term general hospitals in Maine serving a population of approximately one million persons. The average hospital therefore serves a population of approximately 16,667 people.

The *Patient Origin Study* data, however, show substantial variations from this expected average. The largest Maine hospital serves 109,800 people and the smallest 1,400.

The largest of the hospitals, Maine Medical Center with about 400 beds in 1968, is not an exceptionally large hospital by usual standards. Even so, Maine Medical Center serves a population equal to the population served by all 22 of Maine's smallest hospitals combined. These 22 hospitals have a total of 660 beds, which is 260 more beds than Maine Medical Center.

The report continues, "To illustrate it another way, the ten largest hospitals in Maine serve a population equal to the total served by the remaining 50 smaller hospitals."

Patterns of Movement

The study found that there are measurable patterns of patient movement among the hospital communities in Maine. One measure described in the report is the extent of reliance by community residents on their own hospital.

The larger hospitals, naturally, attracted patients from hospital communities other than their own. Smaller hospitals lost patients from their communities to those of the larger hospitals. Isolated hospitals retained a high percentage of the patients from their own communities, and non-isolated hospitals had considerable interchange of patients back and forth with other nearby communities.

Patterns of patient migration are also described in the report. Migration of hospital patients, like many other activity patterns in Maine, follows a general north-to-south flow within the State. Migration also follows a general pattern from smaller communities to larger ones and from isolated communities to non-isolated ones.

The migration patterns shown in the report give a rough measure of the relative strengths of different hospital communities and of their influence upon one another. One indication of the strength of the Portland hospital community, for example, is the fact that it received in-migrations of patients from virtually every other hospital community in the State. Other areas lost patients to some hospital communities at the same time that they received patients from others.

Admission Rates

Specific admissions-per-population rates were calculated for each of the 45 hospital communities in Maine. The state-wide rate was 151 admissions per thousand population.

There was substantial variation from this figure, however. The variance in rates among the 45 hospital communities ranges from a low of 108 admissions per thousand to a high of 266 per thousand.

The State's two largest referral areas, Portland and Bangor, have low admission rates with 122 per thousand for Portland and 109 per thousand for Bangor. Even though these centers served large populations from outside their immediate service areas, the admission rates for the population in their service areas are well below the State average. Thus, the availability of a wide range of services is not necessarily followed by a high local admission rate.

There was substantial variation among regional admission rates, also. The Upper Kennebec Valley admission rate of 190 per thousand, and the Aroostook rate of 177 per thousand, were considerably above the State

average. The Southern Maine Region had the lowest rate at 131 per thousand.

Corollary Observations

In-depth analysis of the patient origin data and indexes yielded significant corollary results, especially on two subjects: admission rates and area of potential hospital consolidation.

Six characteristics were cited as associated with high admission rates:

1. Rural nature of population;
2. Low ratio of doctors to population;
3. Small hospital size;
4. High ratio of beds to population;
5. High investment in hospital construction;
6. Low per diem costs in individual hospitals.

The first two of these factors are especially highly correlated with each other, as are the last four.

Without attempting to state the exact cause and effect relationship between the factors, the report provides a tentative description of the relationships. For the first two factors, the rural nature of an area contributes to the scarcity of doctors, and the scarcity of doctors in turn contributes to an increase in the admission rate.

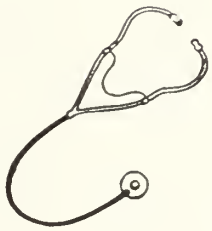
The last four factors appear to relate to the efficiency and economics of hospital operations. Small hospitals are less able to run at an efficient level and therefore need more beds to serve the same population that a larger hospital might serve. This results in a higher ratio of beds per thousand population than in areas with larger hospitals. Because more beds have to be constructed, capital investment must be greater. With a high ratio of beds to population, there are many beds available for patients who may not in reality be acute care patients and who require less than acute care services and facilities. Such patients are less expensive than true acute care patients, and therefore hospitals with larger numbers of these patients can care for them at a lower per diem cost than they can care for true acute care patients.

An additional observation lists eight areas in Maine where two or more hospitals currently compete for the same patients, personnel, and dollars. This strong interrelationship of medical facilities and geographic areas suggests these areas as prime candidates for consolidation of hospital services, personnel, and facilities.

One of the main objectives of the report was to achieve a degree of accuracy sufficient to insure the continuing usefulness of the techniques and results of the study for adaptation to expanded studies in the future. The present report is only a beginning of research into the health care system of the State of Maine.

Summary

There were 60 short term general hospitals in the State of Maine serving approximately 1,000,000 residents in 1968. Maine Medical Center with 400 beds served a population equal to the population served by a combination of 22 of Maine's smaller hospitals which collectively had 660 beds. Maine hospital communities admit an average of 151 persons per year for each thousand of population. The variation runs from a low of 108 per thousand to a high of 266 per thousand. Several factors such as physician to population ratios in given areas, location of facilities and capital investment in facilities, bed to population ratios, and individual hospital per diem costs are cited as being correlated with varying admission rates. The year-long 100% sample used as the basis for this study indicates several areas in the State where two or more hospitals because of common population and intercommunity flow of patients are viewed as being candidates for hospital consolidation.



Dietary Management of the Chronically Uremic Patient*

Our Experiences at Maine Medical Center

Miss Phyllis B. Cushman, R.D.**

The importance of diet therapy in the treatment of kidney failure has been recognized for many years. With the development of the artificial kidney and kidney transplantation, proper dietary restriction has remained important for a number of reasons. With careful dietary management, the length of time between treatments on the artificial kidney may be extended and the total number of treatments and the total cost may be reduced.

Dietary control of kidney failure is not simple. The type and severity of kidney disease varies among individuals, and diet varies to meet these needs. Time may produce variation in the presence and severity of certain symptoms in individual patients, and therapy must change to meet the needs at the particular moment.

Dietary treatments of renal failure, and dialysis can maintain the patient until kidney transplantation is possible.

There are three types of low protein diets in use at present. There is no firm basis for using one of these unless there is objective evidence of nitrogen retention, as in uremia.

The three types of protein diets are:

1. The Low Protein, Low Sodium, Low Potassium Diet.

This diet normally contains 40 grams of *varied* protein sources with a 500-800 mg. (21-35 mEq.) sodium limitation and a 1500 mg. (38 mEq.) potassium limitation. Fluids may or may not need to be restricted. Adjustments in all four components may be made as the condition demands. This diet is most often used in the early stages of uremia and *may* be used when a patient is receiving dialysis.

2. Electro dialyzed whey or E D W diet.

This diet contains E D W,® a low protein commercial product from Wyeth Laboratoryy It is available at present to a few Dialysis Centers for investigational purposes. It is high in calories and low in protein, sodium, and potassium. By using it, dialysis treatments are needed less frequently thus reducing cost and allowing the centers to dialyze more patients. The major difficulty is its poor acceptance by the patients.

3. The Modified Giovanetti Diet

This diet consists of *selected* proteins in the amount of 18 to 20 grams. Sodium, potassium and fluids may or may not be limited according to individual needs. The physiological basis is still not completely understood. However, by providing a delicate balance between essential and non-essential amino acids, it enables the body to use its own wastes efficiently. It is known that the diet cannot be liberalized without upsetting the balance and precipitating a return of symptoms which had been alleviated by adherence to the Modified Giovanetti Diet.

The Maine Medical Center has two Modified Giovanetti Diets available: the first, restricted to 20 grams of selected protein, 800 mg. (35 mEq.) sodium and 1500 mg. (38 mEq.) potassium; the second, restricted to 20 grams selected protein with no limitations on sodium or potassium. We restrict fluids only when ordered. The criteria for fluid restriction is a consideration of the volume of urine formed and the insensible fluid loss. The sodium in diet #1 can be further restricted by using unsalted butter or it can be increased by adding salt in preparation or after preparation of foods. The potassium in diet #1 should not be further restricted as this would reduce calories to inadequacy. A minimum of 2000 calories is essential in order to avoid tissue protein catabolism with its undesirable effects as discussed later.

The selected protein of both Modified Giovanetti Diets consists of 1 egg and 6½ oz. milk providing 13½ grams of protein of high biological value. The remainder of protein is made up of 3 slices of special low protein bread, 1 serving of cereal, and 3 servings of select vegetables. This provides the minimal requirements of essential amino acids except methionine, and as little of the non-essential amino acids as possible. A second egg may be used in place of the milk. Meat, fish and poultry are not used because they contain relatively greater amounts of non-essential amino acids. Endogenous protein turnover is reduced to a minimum by giving only the bare minimum requirements of the essential amino acids daily. In uremia, endogenous urea along with other nitrogenous products can be reutilized in the synthesis of non-essential amino acids if the minimal requirements of essential amino acids and calories are provided in the diet. Some of the "complete" protein foods should be included at each meal to provide the most effective mixture of amino acids.

Calories from carbohydrate and fat sources must be adequate to avoid catabolism of tissue protein as much as possible. The energy needs of the body take priority over other functions. The body normally tends to use carbohydrate as its main source of energy, but if it is not sufficiently available tissue protein catabolism may result. Catabolism of protein adds to the excretory load for urea and potassium. A reduction in tissue break-

*Presented to the Maine Dietetic Association, Oct. 29, 1969.
**Chief Therapeutic Dietitian, Maine Medical Center, Portland, Maine 04102.

down retards the release of potassium from the cells into the extracellular fluid including vascular space. A high potassium blood level threatens cardiac function and may affect the nervous system.

The provision of adequate calories at low protein, low sodium, and low potassium levels is difficult because the selection of foods is so limited. The choice of carbohydrate is critical since significant amounts of protein are present in all the "bulk" carbohydrates. The special low protein bread is essential in this respect. The Maine Medical Center uses Dietetic Paygel P Wheat Starch Flour available from General Mills to make this bread. Other brands available are:

1. Self-Raising Wheat Starch Flour (Mac Dowell Brothers, Ogdensburg, New York). This one is not suitable for restricted sodium diets.
2. Resource Baking Mix** (D. M. Doyle Pharmaceutical Company, Minneapolis, Minnesota).
3. Cellu Lo/Pro Low Protein Baking Mix** (Chicago Dietetic Supply Company, La Grange, Illinois).
4. Low Protein Dry Mix (University of Toronto, Toronto, Ontario).

The special bread made from Dietetic Paygel P Wheat Starch Flour is of unusual texture, almost a cross between bread and cake. It is preferred toasted by most patients. It must, however, be handled with *extreme care* as it crumbles easily. There are other items, desserts and muffins, that may be made, and our diets may be rearranged in the future to include them.

Alcohol is a good source of calories but its use must be balanced against fluid restrictions and local attitudes. D. M. Doyle has another product available which can be figured into the diet and is useful in providing calories with no protein. This product, Controlyte,® when prepared according to the directions on the can provides 370 cc fluid, 1000 calories, 20 mg. (.87 mEq.) sodium and 8 mg. (.20 mEq.) potassium. Between meal feedings are desirable to provide a continuous source of calories thus minimizing tissue catabolism.

The potassium allowed in diet #1 should be spaced throughout the day to avoid sudden blood level increases. Potassium and sodium are found in many foods naturally. Foods with a high content are excluded, where as a limited amount of moderately high content foods may be used to make the diet as palatable as possible. The method of preparation of vegetables affects the potassium content. Raw vegetables usually have a higher potassium content than those cooked in a large amount of water and drained well, because some of the potassium is in the discarded fluid. Draining of canned vegetables and fruits not only reduces fluid but reduces the potassium content to some degree.

**Actually Resource Baking Mix from Doyle Pharmaceutical Company and Cellu Low Protein Baking Mix from Chicago Dietetic Supply Company are the same basic product. It was first made and sold by General Mills, and it is still being made by them but is distributed only by Doyle and Chicago Dietetic Supply House.

Both sodium and potassium are involved in the maintenance of fluid balance. In uremia, fluid intake and fluid output must be carefully balanced. Fluid intake may be normal if no edema is present. Since the malfunctioning kidneys are unable to concentrate and dilute the urine, the excretion of waste products is impaired. Fluid intake may be increased slightly to help the body excrete waste products. Fluids normally need to be decreased late in the course of renal insufficiency. Water may be removed by dialysis, therefore, allowing some patients a higher fluid intake than would otherwise be possible. There are three sources of water to the body; water itself, water contained in foods, and water formed by oxidation of foodstuffs in the body. The latter normally figures about 400 millilitres daily. If fluid retention is extreme, considerable attention to the water content of the food may be required. Within the last three years, however, we have only had to figure the water content of every food for two patients. Normally we need only to eliminate juices, drain fruits and cut down on beverages. As stated earlier, an additional egg could replace the milk if necessary. Fluid allotment should be spaced throughout the day to eliminate thirst.

Nausea and vomiting may initially interfere with acceptance of adequate intake. A blenderized preparation of the diet, therefore, may be better tolerated at first. The major part of the diet may be given in the form of nourishing liquids; gruel, eggnog, fruit juices, melted popsicles and the allowed beverages. We have also been requested to make the diet bland, but this rigidly restricts choices and the monotony is overwhelming. It is impossible to plan a Diabetic Modified Giovanetti Diet since in essence the Modified Giovanetti Diet relies on high carbohydrate foods and the Diabetic Diet necessitates low carbohydrate intake. Sweet foods have been nauseating at first to some patients and this restricts calories too much to make the diet really adequate. Sourballs counteract the sweet yet greasy mouth sensation of which the patient complains, and sourballs are high carbohydrate with nil protein, sodium and potassium. The allowed gingerale often alleviates nausea and headache.

We specify two cups of Casco® gingerale may be used daily. It is not our policy usually to state brand names in diet copies or use them in teaching, but in some cases we find it beneficial. When writing the Modified Giovanetti Diet #1, we decided to test in our laboratories the beverages we were using since we were all aware that the water used in preparing them did make a difference in their sodium and potassium content. Therefore, we specified particular beverages in order to make this strict diet as accurate as possible.

Once chronic renal failure is apparent, reversal of the basic disease process is virtually impossible. Symptoms can be improved however. Soon after the Modified Giovanetti Diet is instigated as therapy; vomiting, nausea, anorexia, and diarrhea rarely occur. It may be necessary to dialyze the patient before therapy is started, and some

physicians feel every patient with severe chronic uremia should be given at least one dialysis. These gastrointestinal symptoms are common in patients on standard low protein diets. Any indiscretion by patients on the Modified Giovanetti Diet usually results in a return of gastrointestinal symptoms within 12-24 hours. The onset of terminal uremia may be delayed for several months. Besides lengthening life, the Modified Giovanetti Diet makes the patient feel better and he may even be able to work. The diet is helpful in prolonging the time before repeated dialysis is necessary and sometimes decreases frequency of treatments once they are started.

Treatment by diet is essential even though dialysis removes accumulated wastes. Greater freedom in intake to some degree may be possible but a controlled diet reduces potentially harmful changes in blood composition between treatments. For instance, by controlling sodium, excessive fluid accumulation between treatments is avoided. Thus high blood pressure is avoided, and the chance of congested lungs and edema is lessened.

There are some disagreements still in regard to dietary treatment for these patients. One is related to treatment on dialysis days. Some feel strongly that diet therapy should not be disregarded at this time because complications might arise, and because they feel it is too difficult for the patient to readjust to the strict diet. Others feel three eggs should be added, and the electrolyte and fluid restriction may be lessened on dialysis days. The eggs they feel compensate for the protein loss.

There are still some unresolved problems. Previously we stated that the methionine requirement was not met by the diet. Some feel, therefore, that 250 milligrams of methionine should be given twice daily as a supplement. Some references, however, state that there is no evidence that the supplement improves the patients' condition. In some cases anemia, invariably a symptom of uremia, is increased when the Modified Giovanetti Diet is utilized; in other cases it is decreased. It also does not often respond to vitamin and iron supplementation. The physician may wish to prescribe iron, calcium, and B complex vitamins, especially folic acid as supplements since the diet is apt to be deficient in these nutrients. Thiamine aids in the metabolism of carbohydrate.

A low protein diet is difficult for many people to accept especially since most Americans are great protein consumers. Most people eat more than is necessary for good health. The Modified Giovanetti Diet is hard to accept since it is so restricted. The Physician and Dietitian must work cooperatively; the physician explaining the purpose of the diet adequately and repeatedly, the dietitian teaching the diet and aiding in meal planning. Those patients who are best informed about their disease and its treatment are most able to receive benefits from the diet and from dialysis. Enthusiasm on our part is a must. Motivation of the patient is extremely important. Teaching should be started early. The patient and his family should be taught about food composition, the reasons for exclusion or inclusion of specific foods, and the importance of reading labels if sodium and potassium are restricted. Follow-up upon discharge is essential. The preferred schedule is every week for 2-3 months, then every three months if the patient is getting along well. The discharged patient must assume the ultimate responsibility of adhering to the prescribed diet and of keeping his follow-up appointments. If the Dietitian and the Physician have done their duty and have taught him well, it is his choice and his life.

Appendix

Modified Giovanetti (Giordano) Diet #1

This Modified Giovanetti Diet may be used for selected patients with renal failure. The diet is planned to supply enough protein in food eaten to minimize breakdown of body stores of protein; to provide the essential amino acids; to minimize the intake of the nonessential amino acids; to maintain caloric equilibrium; and to adjust electrolyte imbalance. The diet is essentially high carbohydrate, low protein (20 gms.), moderate fat (minimum 2000 calories), low sodium (800 mg.), and low potassium (1500 mg.). The diet is deficient in iron, calcium, phosphorus, and the B complex vitamins, therefore the physician may wish to prescribe supplements.

The aim is to provide all the essential amino acids in the allowance of 1 egg and 6½ ounces of milk daily. The other calories are in the form of carbohydrate and fat, as protein free as possible.

Three meals and in-between meal beverages have been planned. It is essential that the diet be consumed in full. However, some other item may be saved for in-between feeding if desired.

FOODS TO BE INCLUDED:

- Milk – 6½ ounces daily
- Egg – 1 daily
- Cereal – 1 unsalted serving chosen from:
  - Cornflakes 1 cup (Van Brode)
  - Cream of Rice ½ cup
  - Cream of Wheat ½ cup
  - Puffed Rice 1 cup
- Bread – 3 slices Special Low Protein Bread
- Vegetables – 2 from List A and one from List B (in amounts stated). Use fresh, canned without salt, or frozen if no salt or sodium has been used in processing.
- Fruits – 4 servings (in amounts stated).
- Desserts – 2 popsicles, 8 sourballs and 5 butterballs.
- Beverages – 1 cup (150cc) tea, 2 cups (240cc) Casco gingerale, 1 cup (240cc) Snow Crop frozen lemonade (reconstituted as directed), and 1 cup (240cc) Coca Cola or Pepsi Cola or ½ cup (120cc) Cranberry juice.
- Fats – 5 tsp. butter or margarine.
- Miscellaneous – Sugar, honey, maple syrup and jelly as desired to increase calories; pepper, bay leaves, caraway, cinnamon, garlic, ginger, dry mustard, nutmeg, oregano, paprika, parsley, rosemary, and tarragon in moderation for flavor.

FOODS AVOIDED:

- Milk – Any in excess of 6½ oz. allowed. Buttermilk, cream.
- Eggs – Any in excess of 1 allowed.
- Cheese – All.
- Meats, Fish, Poultry – All.
- Cereals – Any in excess of 1 serving allowed. Any kinds not

listed in Allowed list. Spaghetti, noodles, macaroni, and rice.
Bread – All except 3 slices Special Low Protein Bread.
Vegetables – Any in excess of the three servings allowed. Baked beans, beet greens, carrots-raw, celery, dandelion greens, kale, Lima beans, legumes, lentils, mushrooms, peas, potato chips, potatoes-French Fried, soybeans, spinach, and Swiss chard.
Fruits – Any in excess of 4 servings allowed. Avocados, dates, melons (except watermelon), prunes, and raisins.
Desserts – Cakes, cookies, custard, gelatin, ice cream, junket, pies, puddings, and sherbet (unless water ice).
Soups – All. Bouillon cubes.
Beverages – Milk (in excess of 6½ oz. daily allowance), buttermilk, cocoa, coffee; tea, Coca Cola, gingerale, Pepsi Cola in excess of servings allowed; other carbonated beverages.
Fats – Salad dressings and peanut butter.
Miscellaneous – Commercial baking powder, baking soda, salt, vegetable salts, salt substitutes, Accent, condiments, pickles, olives, nuts, and popcorn.

Sample Menu

Breakfast
½ cup Apple juice
½ cup Cream of Rice
1 tbsp. Honey
1 slice Special bread
1 tsp. Butter
1 tbsp. Jelly
3½ oz. Milk
150cc. Tea
Sugar

Lunch
1 sf Poached egg
½ cup sf Wax beans (canned)
⅓ cup sf Beets (fresh)
½ med. Bk. white Potato
1 slice Special bread
3 tsp. Butter
1 tbsp. Jelly
1 cup Gingerale
1 Popsicle

Dinner
Fruit Bowl
¼ sm. banana
1 cup Blueberries
1 sm. Peach (fresh)
1 slice Special bread
1 tsp. Butter
1 tbsp. Jelly
1 cup Pepsi Cola
1 Popsicle
Sugar
3 oz. Milk

In-betweens
8 Sourballs
5 Butterballs
1 cup Gingerale
1 cup Lemonade with
1 tbsp. Honey

Breakfast
½ cup Strawberries
1 cup Cornflakes
1 slice Special bread
1 tsp. Butter
1 tbsp. Jelly
3½ oz. Milk
150cc. Tea
Sugar

Lunch
1 Hard cooked egg
⅓ cup sf Carrots (cooked, fresh)
½ cup sf Green beans (canned)
1 sm. raw Tomato
1 slice Special bread
3 tsp. Butter
1 tbsp. Jelly
1 cup Gingerale with
1 tbsp. Honey
1 Popsicle

Dinner
Fruit Plate
½ cup Pear (canned)
½ cup Pineapple (canned)
¼ cup Apricots (canned)
1 slice Special bread
1 tsp. Butter
1 tbsp. Jelly
1 cup Coca Cola
1 Popsicle
Sugar
3 oz. milk

In-betweens
8 Sourballs
5 Butterballs
1 cup Gingerale with
1 tbsp. Honey
1 cup Lemonade

List A Vegetables – approximately 1 gm. Pro., 120 mg.K and 11 mg. Na.

Beans, Green or Wax		Green Peppers	
Canned	½ cup	Cooked, fresh	1 med.
Cooked, fresh	⅓ cup	Raw	1 med.
*Beets		Lettuce	3 lg. leaves
Canned	¼ cup	Onions	
Cooked, fresh	⅓ cup	Cooked, fresh	½ cup
Cabbage		Raw	1 (2 inch)
Cooked, fresh	½ cup	Radishes	
Raw	½ cup	Raw	4
*Carrots		Rutabagas	
Canned	½ cup	Cooked, fresh	½ cup
Cooked, fresh	⅓ cup	Summer Squash	
Cucumbers		Cooked, fresh	½ cup
Raw	⅓ large	*Turnip	
Eggplant		Cooked, fresh	⅓ cup
Cooked, fresh	⅓ cup		

List B Vegetable – approximately 2 gms. Pro., 230 mg. K and 5 mg. Na.

Asparagus		Parsnips	
Canned	6 spears	Cooked, fresh	½ cup
Cooked, fresh	6 spears	*Potatoes, Sweet	
Broccoli	1 stalk	Cooked	½ cup or 1 medium
Brussels Sprouts		*Potatoes, White	
Frozen	½ cup	Canned	1 medium
Cauliflower		Cooked, pared	1medium
Cooked, fresh	½ cup	Cooked, in skin	½ medium
Raw	½ cup	Tomatoes	
Corn		Canned	½ cup
Canned	½ cup	Raw	1 small
Cooked, fresh	½ cup	Juice	½ cup
Okra			
Cooked, fresh	9 pods		
Raw	8 pods		

*Do not use more than one starred item daily.
Discard cooking water.
Vary your vegetables from day to day to be certain you meet your nutrient needs.

Fruits – approximately 135 mg. K and 2 mg. Na.

Apple, raw	1 small	*Papayas	⅓ cup
Apple juice	½ cup	Peach, canned	⅓ cup
Applesauce	¾ cup	*Peach, fresh	1 small
*Apricots, canned	¼ cup	Peach nectar	⅔ cup
Apricot nectar	⅓ cup	Pear, canned	½ cup
Banana	¼ small	*Pear, fresh	1 small
Blackberries	¾ cup	Pear nectar	1 cup
Blueberries	1 cup	Pineapple, canned	½ cup
Cherries, canned	⅓ cup	Pineapple, fresh	⅔ cup
Cherries, raw	½ cup	Pineapple juice	⅓ cup
*Figs, fresh	2 small	Plums, canned	½ cup
Fruit cocktail	⅓ cup	Plums, fresh	1 med.
*Grapefruit, canned	½ cup	*Prune juice	¼ cup
*Grapefruit, fresh	½ small	Raspberries, Red, fresh	⅔ cup
Grapefruit juice	⅓ cup	Raspberries, Black, fresh	½ cup
Grapes, fresh	½ cup	Strawberries, fresh	½ cup
Grape juice	⅓ cup	Tangerine, fresh	1 small
*Lemon juice	½ cup	*Tangerine juice	⅓ cup
Lime juice	½ cup	Watermelon	⅔ cup
Orange, fresh	½ small		
*Orange juice	⅓ cup		

*Do not use more than one starred item daily.
Vary your fruits from day to day to be certain you meet your nutrient needs.

SPECIAL LOW PROTEIN BREAD

Paygel P Wheat Starch (DPP Wheat Starch) is available from

General Mills, Inc., Specialty Products Division, 9200 Wayzata Boulevard, Minneapolis, Minn. 55440. It is packed in No. 10 tins (enough for approximately 4 loaves). Cost $2.50 post paid for one can and $13.50 for one case of six cans. Delivery time is approximately 2 weeks. Sodium-free baking powder can be obtained from the pharmacist without a prescription.

The recipe is:

Tartaric acid	7.5 gms.
Potassium bi-tartrate	56.1 gms.
Potassium bi-carbonate	39.8 gms.
Cornstarch	28.0 gms.

Bread Recipe – 1 loaf, 27 slices (3/8") thick

1 tbsp. sugar	½ tsp. salt
1¼ cups warm water	2¾ cups DPP Wheat Starch
1 pkg. dry active yeast	¼ cup hydrogenated shortening
3 tbsp. sugar	
¾ tsp. Na free baking powder	

Place 1 tbsp. sugar and water in a large mixer bowl. Add yeast and stir until dissolved; let stand five minutes. Add dry ingredients and shortening. Beat at low speed, scraping sides of bowl until ingredients are moistened; then beat 1 minute at high speed, scraping sides of bowl with rubber spatula. Scrape sides of bowl; cover with towel and let stand at room temperature for 30 minutes. Grease loaf pan, 9 x 5 x 2¾" or 8½ x 4½ x 2 5/8"; set aside. Beat bread mixture down, approximately 25 strokes; pour into greased loaf pan. Cover with towel and let stand at room temperature for 30 minutes. Heat oven to 375°. Bake 55 minutes. Cool bread thoroughly. Refrigerate 1-2 hours after it has reached room temperature.

NOTE:
Do not pack flour. If bread mixture is like pie crust, add 1-2 tbsp. water; if like pancake batter, add 1-2 tbsp. DPP Wheat Starch. Cover opened can of flour carefully with aluminum foil. To cut bread, use a serrated or an electric knife and cut from bottom to top. Freeze any portion of bread which cannot be eaten in two days – wrap and seal carefully. To thaw, let stand at room temperature 3-4 hours.

Butterball Recipe
Butterballs are made like butter frosting. The approximate recipe for 50 is ¼ lb. butter, 2 cups confectionery sugar and vanilla to flavor. There should be enough sugar to form firm balls when mixture is rolled out. Balls should be thoroughly chilled.

RECIPES FOR MODIFIED GIOVANETTI DIET

Onion Scrambled Egg

1 tbsp. chopped onion	1 egg (+2 tsp. water-optional)
1 tsp. butter	pepper to taste

Melt butter in a small frying pan. Saute onion until tender. Slightly whip egg (with water). Pour over the onion and scramble. Serve at once.

Hash Brown Potato (Use as 1 B vegetable and 2 butter)

1 small cold boiled potato	2 tsp. butter
2 tbsp. chopped onion	pepper to taste

Peel and grate potato. Melt butter in a small frying pan. Add onion and potato and fry over medium heat; turn occasionally to obtain desired brownness.

Carrots with Herbs

½ cup canned carrots	dash of pepper
1 tsp. butter	dash of nutmeg
2 tsp. water	dash of chopped parsley
¼ - ½ tsp. sugar	dash of tarragon

Saute carrots in butter, water and sugar by shaking pan and stirring constantly. When hot, add seasonings and serve.

Fresh Fruit Compote
Make a light syrup of 1 cup sugar, 1 cup water, a piece of lemon rind and a stick of cinnamon. Cut apples and pears in quarters and cook until fruit is tender. Measure out your allowed servings.

Other Suggestions for Use of Herbs with Vegetables
Summer Squash with Nutmeg
Summer Squash with Butter, Sugar and Cinnamon
Broccoli with Oregano

Modified Giovanetti (Giordano) Diet #2

This Modified Giovanetti Diet may be used for patients with renal failure when abnormal retention of sodium and potassium is not present. The diet is planned to supply enough protein in food eaten to minimize breakdown of body stores of protein; to provide the essential amino acids; to minimize the intake of the nonessential amino acids; and to maintain caloric equilibrium. The diet is low in protein (20 gms.) with liberal use of pure carbohydrate and fat to provide a minimum of 2000 calories. The diet is apt to be deficient in iron, calcium, phosphorus, and the B Complex vitamins, therefore the physician may wish to prescribe supplements.

FOODS TO BE INCLUDED:
- Milk – 6½ ounces daily.
- Egg – 1 daily
- Cereal – 1 serving chosen from: ½ cup Cream of Rice, Cream of Wheat, Oatmeal, Rolled Wheat, Bran flakes, Wheaties; 1 cup Cornflakes, Puffed Rice, Puffed Wheat, Rice Krispies; 1 large biscuit Shredded Wheat.
- Bread – 3 slices Special Low Protein Bread
- Vegetables – two from List A, one from List B (in amounts stated).
- Fruits – As desired except avocado. Use sweetened often to add calories.
- Desserts – Fruit or popsicles.
- Beverages – Coffee, tea, carbonated beverages, lemonade and Kool-Aid.
- Fat – Butter, margarine and oils as desired-use freely to increase calories.
- Miscellaneous – Sugar, honey, syrups, jam, jelly, hard candy as desired to increase calories; salt, pepper, vinegar, and spices as tolerated.

FOODS AVOIDED:
- Milk – Any in excess of 6½ oz. allowed. Cream.
- Eggs – Any in excess of 1 allowed.
- Cheese – All.
- Meats, Fish, Poultry – All.
- Cereals – Any in excess of 1 serving allowed. Any kinds not listed. Spaghetti, noodles, macaroni, and rice.
- Bread – All except 3 slices Special Low Protein Bread.
- Vegetables – Any in excess of the three servings allowed. Baked beans, Lima beans, legumes, lentils, peas, and soybeans.
- Fruits – Avocado.
- Desserts – Cakes, cookies, custard, gelatin, ice cream, junket, pies, puddings, and sherbet (unless water ice).
- Soups – All.
- Beverages – Milk (in excess of 6½ oz. daily allowance), milk drinks, and cocoa.
- Fats – Mayonnaise and peanut butter.
- Miscellaneous – Nuts.

Sample Menu

Breakfast
1 sm. Banana
½ c. Cream of Wheat
1 tbsp. Honey
1 slice Special bread
1 tsp. Butter
1 Jelly
3½ oz. Milk
Coffee
Sugar

Lunch
1 Poached egg
½ cup Wax beans
½ cup Beets
1 med. White potato
5 tsp. Butter
1 slice Special bread
1 Jelly
Tea
Sugar
1 Popsicle

Dinner
Fruit Plate
Apple wedges
Peach slices
Pear halves
1 slice Special bread
1 tsp. Butter
1 Jelly
Tea
Sugar
1 Popsicle
3 oz. Milk

In-betweens
10 A.M. Pineapple juice
3 P.M. Gingerale with Honey
H.S. Lemonade

Breakfast
½ cup Prune juice
1 cup Cornflakes
1 slice Special Bread
1 tsp. Butter
1 Jelly
3½ oz. Milk
Coffee
Sugar

Lunch
1 Soft cooked egg
½ cup Carrots
½ cup Green beans
1 small Sweet potato
5 tsp. Butter
1 slice Special Bread
1 Jelly
1 cup Gingerale with Honey
1 Popsicle

Dinner
Fruit Plate
Pineapple chunks
Apricot halves
Grapes
1 slice Special bread
1 tsp. Butter
1 Jelly
Tea
Sugar
1 Popsicle
3 oz. Milk

In-betweens
10 A.M. Grape juice
3 P.M. Gingerale with Honey
H.S. Lemonade

List A Vegetables

Beans, Green or Wax	½ cup	Lettuce	4 large leaves
Beets	½ cup	Onions	½ cup
Beet greens	⅓ cup	Parsnips	⅓ cup
Cabbage	½ cup	Green Peppers	1 large
Carrots	½ cup	Radishes	4
Celery	2 stalks	Rutabagas	½ cup
Chard	⅓ cup	Summer Squash	½ cup
Cucumbers	⅓ 7″	Tomatoes	½ cup
Eggplant	½ cup	Turnips	½ cup

List B Vegetables

Asparagus	6 spears	Okra	½ cup
Broccoli	1 stalk	Potatoes, White	1 med.
Brussels Sprouts	⅓ cup	Potatoes, Sweet	1 small
Cauliflower	1 cup	Spinach	⅓ cup
Corn	½ cup	Winter Squash	½ cup

SPECIAL LOW PROTEIN BREAD

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Recipe – 1 loaf, 27 slices (3/8″ thick)

1 tbsp. sugar
1¼ cups warm water
1 pkg. dry active yeast
3 tbsp. sugar
½ tsp. double acting baking powder
1 tsp. salt
2¾ cups DPP Wheat Starch
¼ cup hydrogenated shortening

Place 1 tbsp. sugar and the water in a large mixer bowl. Add yeast and stir until dissolved; let stand 5 minutes. Add dry ingredients and shortening. Beat at low speed, scraping sides of bowl until ingredients are moistened; then beat 1 minute at high speed, scraping sides of bowl with rubber spatula. Scrape sides of bowl; cover with towel and let stand at room temperature for 30 minutes. Grease loaf pan, 9 x 5 x 2¾″ or 8½ x 4½ x 2 5/8″, set aside. Beat bread mixture down, approximately 25 strokes; pour into pan. Cover with towel and let stand at room temperature for 30 minutes. Heat oven to 375°. Bake 55 minutes. Cool bread thoroughly. Refrigerate 1-2 hours after it has reached room temperature.

NOTE:

Do not pack flour. If bread mixture is like pie crust, add 1-2 tbsp. water; if like pancake batter, add 1-2 tbsp. DPP Wheat Starch. Cover opened can of flour carefully with aluminum foil. To cut bread, use a serrated or an electric knife and cut from bottom to top. Freeze any portion of bread which cannot be eaten in two days – wrap and seal carefully. To thaw, let stand at room temperature 3-4 hours.

ACKNOWLEDGMENT

The author would like to acknowledge the assistance of W. H. Austin, M.D. in reviewing and making suggestions regarding the manuscript. He notes that in our experience the BUN may be a less sensitive index of renal function while the diet is being used and creatinines should be followed as an alternative.

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Competitive Athletics for Children of Elementary School Age*

American Academy of Pediatrics; Committee on the Medical Aspects of Sports, American Medical Association; The American Association for Health, Physical Education and Recreation; and The Society of State Directors of Health, Physical Education, and Recreation

Competitive sports organized by school or other community agencies are now played so universally in all parts of the country by children 13 years of age and younger that the above organizations wish to suggest positive and realistic guidelines to govern participation.

Children of this age are not miniature adults; they are boys and girls in the process of maturation into adults. They seek and can profit from suitable play opportunities, but the benefits are not automatic. High quality supervision and a broad range of physical education activities, including sports adapted to the needs and capacities of growing children, are required for full realization of benefits.

A variety of competitive sports, appropriately a part of a sound physical education program, has the advantage of directing funds, facilities, instruction, and leadership toward all children in the school system or community. Such a program avoids providing a narrow sports experience for children or one directed only to the physically gifted, the well developed, the skillful, or the precocious child.

The problems involved are sufficiently significant and variable to warrant each community's having a local committee representing education, recreational, and medical specialists. Decisions about all school or community athletic programs may then be made in terms of local interest and needs, adequate supervision, and assurance of proper safeguards. Such decisions about athletic programs for children of elementary school age should embody local consideration of the following:

1. Proper physical conditioning.
2. Conduct of the sport: (a) competent teaching and supervision with regard for the relative hazards of each particular sport; (b) modification of rules, game equipment and facilities to suit the maturity level of the participants; (c) qualified officials.
3. Careful grouping according to sex, weight, size, skill and physical maturation when indicated.
4. Good protective equipment, properly fitted.
5. Well-maintained facilities suitable for the sport involved.
6. Proper delineation of the spheres of authority and responsibility for school administration, family, sponsor, physician, coach and athlete.
7. Adequate medical care: (a) periodic health appraisal of children, including a careful health history (see *American Medical Association's Guide for Medical Evaluation of Candidates for School Sports*);† (b) a physician present or readily available during games and practices; (c) established policies, procedures, and responsibilities for: first aid and referral of injured athletes, definitive treatment and follow-up, and evaluation and certification for return following injury or illness; (d) Attention to matters of physical and emotional fatigue and stress, especially of a cumulative nature or effect; and (e) use of the *American Medical Association's Standard Nomenclature of Athletic Injuries** to facilitate reporting and analysis of injuries and illnesses.
8. Salient educational and recreational considerations include:

(a) prerequisites before an inter-school athletic program is started: (1) provision for daily physical education instruction for all children, under the supervision of certificated physical education teachers, (2) opportunities for every child in the upper elementary grades to participate in an organized and supervised intramural athletic program, (3) and assurance that the athletic program will not curtail the time or budget of the normal school program (i.e., will not utilize school time, facilities, personnel or funds in any way which would jeopardize the total educational experience of the participants or of other children);

(b) program for interschool or community athletics: (1) participation limited to children in the upper elementary grades, (2) parental permission for each child, (3) qualified leadership for the planning and conduct of competitive athletic programs for children, (4) a schedule of contests (frequency and hour) appropriate for children of this maturity level, (5) the activities limited to a neighborhood or community basis without play-offs, bowl contests, or all-star contests, and (6) *Avoidance of undesirable corollaries to organized competitive athletics, such as excessive publicity, pep squads, commercial promoting, victory celebrations, elaborate recognition ceremonies, paid admission, inappropriate*

*As used in this Statement, "elementary school age" is synonymous with "in grades 1 through 6," "13 years of age and younger," and "preadolescent."

This statement was prepared jointly by the above organizations.

Reprinted from Pediatrics, Vol. 42, No. 4, October, 1968.

†American Medical Association, 535 N. Dearborn, Chicago, Illinois 60610.

spectator behavior, high pressure public contests and exploitation of children in any form.

The positive values of sports should be emphasized because of their important effects on stamina and physiologic functioning and because of their lifelong value as recreational activities. Examples of sports appropriate for children of elementary school age are archery, bowling, golf, skating, swimming, tennis, and track.

Boxing has no place in programs for children of elementary school age because its goal is injury and because the educational benefits attributed to it can be realized through other sports.

Sports with varying degrees of collision risk include baseball, basketball, football, ice hockey, soccer, softball, and wrestling. The hazards of such competition are debatable. The risks are usually associated with the conditions under which practice and play are conducted and the quality of supervision affecting the participants.

Unless a school or community can provide exemplary supervision – medical and educational – it should not undertake a program of competitive sports, especially collision sports at the preadolescent level.

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Physicians' Services In The Outpatient Department

When a physician sees a patient in the outpatient department, it is difficult to properly evaluate the allowable charges under Medicare, Part B, if the physician does not indicate the circumstances involved. If the physician's charge is greater than that of a routine hospital visit, the claim form should indicate the extent of care, the time involved, and whether or not the outpatient call was an emergency.

Generally, if a physician schedules a visit at the outpatient department, his office is at the hospital, or he spends a set day at the clinic for visits, the allowable Medicare benefits will be equal to the physician's usual and customary charge for a routine hospital call. However, if the physician is called to the outpatient department from his rounds in the hospital, or his office or home, the allowable Medicare benefits may be higher if the Request for Payment form is properly documented. — **From Medicare Health Insurance Part B, Box 4629, Portland, Maine.**

SEX

The role of the physician changes from time to time and is dependent upon many variables. We are in a most unique position, for although our job is to relieve suffering and stave off death, we can at best only temporize, since all of our patients are going to die someday of something. We are one of the few callings who are in business to do ourselves out of business. Our greatest accomplishments have really been in the field of prevention, of keeping a disease, a disability, or a dysfunction, from occurring in the first place. It seems odd, then, that we, the preventers, the healers, would do so little about a preventable phenomenon which kills about 60,000 men, women, and children a year, and injures about 4.5 million.

What really is our responsibility and what are we doing about it? It would appear that our responsibility is great as we see the horrible results and know that practically all of these occurrences are preventable. Unfortunately, we do not seem to be doing too much about seeing to it that they do not take place.

Modern Medicine published a series of articles this spring about "The Physicians' Role in Highway Safety" and the Travelers Insurance companies have just sent out a booklet called "Was It Sudden?" They both point out ways we can help to reduce the accident rate with its concomitant pain and anguish. They suggest that simply to blame the car, the driver, alcohol, poor roads, or any one single cause is far from a scientific approach. The causes of accidents are many and work in a "system," or chain reaction to cause a tragic or happy ending to a driving experience. There is a car in more or less good condition, there is you, tired, awake, worried or relaxed, on a road well-lighted or dark, wet or dry, and then add or take away any one of another thousand or more factors, and you may have some leads as to the causes of accidents.

What then can you and I do about applying good scientific methods to accident prevention? Some of the suggestions we can follow to help prevent accidents ourselves include always, and in all ways, driving defensively, maintaining our cars in the best possible shape, and insisting on owning all optional safety devices, including the proper tires at the proper inflation for your car. Limit your driving when tired, emotionally upset or drinking. Adjust your driving and speed to current conditions of highway, weather, traffic or other conditions. Don't rush, keep your temper, and personally, in your own community, support better law enforcement, highway improvement, driver education in the schools and improved driver licensing. Be firm about your patient's medical disability which should keep him or her from driving a car.

Now how can we help prevent injury in the case of the so-called "second collision," that is, the passenger colliding with the inside of the car? First and foremost, *use* the seat belt and shoulder harness. Insist upon buying that car and driving that car with the greatest number of safety features, such as padded dash, collapsible steering wheel and head supports, and always remember, the higher the speed, the greater the severity of the accident.

There are misconceptions in the minds of some people which we must help put aright. For example, some have suggested that a seat belt would prove fatal in case of fire or submerging. The facts are that the chances of survival are greatly increased with the use of the seat belt as the passenger has been protected from the second collision and is, therefore, much more likely to be conscious and able to escape. In every discussion of safety, there is usually one person who knows of someone who was thrown out of a car and suffered only minimal injuries. For every one of those who can show you 10 whose lives were saved by being belted in. And so on and on with feeble excuses not to face the obvious fact that you and your family can be killed, or maimed, in your own car today. If you carry insurance on your car for fear it might be damaged, take out some safety insurance with yourself, for fear you and yours might be damaged. There is a shortage of doctors. Please don't be afraid to be afraid.

Oh, yes, if you have wondered why this editorial was entitled "Sex," be honest, now – would you have read it at all if it had been called "Automotive Safety?"

WILLIAM K. KELLER, M.D.
Chairman, KMA Committee
on Highway Safety

Reprinted from The Journal of the Kentucky Medical Association—September, 1967.

PROTEIN CONTENT / 7 oz. Serving*

Bean with Bacon	6.8	Green Pea with Ham (Frozen)	7.6
Beef	8.0	Hot Dog Bean	8.4
Chicken Broth	5.5	Pepper Pot	6.1
Chicken 'N Dumplings	5.8	Split Pea with Ham	10.2
Chili Beef	6.2	Vegetable Beef	5.0
Green Pea	6.9	Vegetable with Beef (Frozen)	5.4

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Only Flagyl has been able to achieve rates of cure consistently above 90 per cent and often up to 100 per cent in trichomonal infections in both men and women.

Indications: For the treatment of trichomoniasis in both male and female patients and the sexual partners of patients with a recurrence of the infection provided trichomonads have been demonstrated by wet smear or culture.

Contraindications: Evidence of or a history of blood dyscrasia, active organic disease of the central nervous system and the first trimester of pregnancy.

Warnings: Use with discretion during the second and third trimesters of pregnancy and restrict to patients not cured by topical measures. Flagyl (metronidazole) is secreted in the breast milk of nursing mothers. It is not known whether this can be injurious to the newborn.

Precautions: Mild leukopenia has been reported during Flagyl use; total and differential leukocyte counts are recommended before and after treatment with the drug, especially if a second course is necessary. Avoid alcoholic beverages during Flagyl therapy because abdominal cramps, vomiting and flushing may occur. Discontinue Flagyl promptly if abnormal neurologic signs occur. There is no accepted proof that Flagyl is effective against other organisms and it should not be used in the treatment of other conditions. Exacerbation of moniliasis may occur.

Adverse Reactions: Nausea, headache, anorexia, vomiting, diarrhea, epigastric distress, abdominal cramping, constipation, a metallic, sharp and unpleasant taste, furry or sore tongue, glossitis and stomatitis possibly associated with a sudden overgrowth of *Monilia,* exacerbation of vaginal moniliasis, an occasional reversible moderate leukopenia, dizziness, vertigo, drowsiness, incoordination and ataxia, numbness or paresthesia of an extremity, fleeting joint pains, confusion, irritability, depression, insomnia, mild erythematous eruptions, "weakness," urticaria, flushing, dryness of the mouth, vagina or vulva, vaginal burning, pruritus, dysuria, cystitis, a sense of pelvic pressure, dyspareunia, fever, polyuria, incontinence, decrease of libido, nasal congestion, proctitis, pyuria and darkened urine have occurred in patients receiving the drug. Patients receiving Flagyl may experience abdominal distress, nausea, vomiting or headache if alcoholic beverages are consumed. The taste of alcoholic beverages may also be modified.

Dosage and Administration: *In the Female.* One 250-mg. tablet orally three times daily for ten days. Courses may be repeated if required in especially stubborn cases; in such patients an interval of four to six weeks between courses and total and differential leukocyte counts before, during and after treatment are recommended. Vaginal inserts of 500 mg. are available for use, particularly in stubborn cases. *When the vaginal inserts are used* one 500-mg. insert is placed high in the vaginal vault each day for ten days and the oral dosage is reduced to two 250-mg. tablets daily during the ten-day course of treatment. Do not use the vaginal inserts as the sole form of therapy. *In the Male.* Prescribe Flagyl only when trichomonads are demonstrated in the urogenital tract, one 250-mg. tablet two times daily for ten days. Flagyl should be taken by both partners over the same ten-day period when it is prescribed for the male in conjunction with the treatment of his female partner.

Dosage Forms: Oral tablets . . . 250 mg.
Vaginal inserts . . 500 mg.

*References available on request.

SEARLE P. O. Box 5110 Chicago, Illinois 60680 942

Research in the Service of Medicine

Owner Breaks Arm When Yacht Runs Agroun

Schuyler, Oct. 31. Harry Waters of Covesville incurred a fractured arm ... acht ... ck a large rock tially capsized. The fire depar had to rescue Waters by small Damage to the yacht is estima

Hasn't the skipper had enough excitement for one day?

For the patient who has been through an accident, the worry and anxiety following the mishap may actually heighten the perception of pain. This is why there's a classic ¼ grain *sedative* dose of phenobarbital in Phenaphen with Codeine—to take the nervous "edge" off, so the rest of the formula can control the pain more effectively.

A.H. Robins Company, Richmond, Va. 23220 A·H·ROBINS

Phenaphen® with Codeine

Phenaphen with Codeine Nos. 2, 3, or 4 contains: Phenobarbital (¼ gr.), 16.2 mg. (warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Hyoscyamine sulfate, 0.031 mg.; Codeine Phosphate, ¼ gr. (No. 2), ½ gr. (No. 3), or 1 gr. (No. 4) (warning: may be habit forming).

The compound analgesic that calms instead of caffeinates

Indications: Phenaphen with Codeine provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

DEAN H. FISHER, M.D.
COMMISSIONER

State Of Maine

Department of Health and Welfare

Laboratory Diagnostic and Reference Services in Virology in the State of Maine

MARION C. LACHANCE*

The viral diagnostic services of the Public Health Laboratory in the Maine Department of Health and Welfare are available, free of charge, to residents of the State of Maine through the agency of physicians, health officers and others, who may submit virus specimens in their behalf. To facilitate satisfactory collection and transportation of virus specimens for laboratory examination, personnel in the Virology section assemble and furnish containers designed specifically for viral samples. Commencing June 1, 1970, two such specimen containers will be available to physicians and hospital laboratories, free of charge, upon request to the Public Health Department Laboratory. An appropriate form is enclosed in each container assembly (one per tube or vial) to identify the specimen, patient, physician or hospital and to indicate suspected diagnosis and tests desired. Success of the virus laboratory will be governed strongly by the type of specimen submitted and to some extent by the accuracy of the information provided. An accurate clinical history is an important indication of viral etiology and a prime requisite in interpreting serologic results.

The rubella HAI test program and vaccination of children and non-pregnant, non-protected young females is already well-established and fully operative in the State of Maine. The growing number of requests to the Virology Diagnostic Section for rubella HAI tests prompted the development of a separate one-tube, double-walled mailer for the collection and transport of blood samples for rubella HAI tests. Such specimens (6-8 ml blood) should be accompanied by information concerning the patient's age, date of last monthly period, date of exposure to rubella and presence or absence of a rash at the time the specimen was obtained. A space is also provided on the new rubella form for indicating whether the serum sample is an acute serum (S1), convalescent serum (S2) or whether the serum was collected at some time after the convalescent serum (S3). If the physician's intention is to evaluate the immune status of the patient with regard to rubella virus, a single blood sample is sufficient. Customarily, acute phase sera and convalescent sera are examined simultaneously for evidence of significant differentials in antibody titer; therefore, if a physician seeks an evaluation of immune status only, it would be helpful if this could be indicated on the form provided in the rubella HAI test container. Positive evidence of current or recent infection with rubella virus can only be demonstrated when the titer of specific antibodies in the convalescent serum is at least four-fold higher than the titer in acute phase serum. By and large, the identity of the viral etiologic agent of a current illness necessitates both serology and virus isolations. A single acute phase serum has minor significance in viral diagnosis.

At the present time, rubella virus isolations are limited to rubella syndrome infants. Adequate evidence of the immune status of a pregnant, exposed female can be obtained from the HAI test. Benefits derived from rubella virus isolations, in such cases, are negligible. Isolations from cerebrospinal fluids and/or throat washings of suspect infants should be made during the first month after birth. It is preferable to base a diagnosis of active infection with rubella virus in the infant on results of the HAI test performed on paired sera. The first sera or cord blood should be collected as soon after birth as possible; the second sera should be collected 2-3 months after the birth date. Evidence[1] indicates that a baby will not display a significantly elevated antibody titer to rubella virus after 2 months unless he is synthesizing his own antibody. Virus isolations may also be warranted if a strong possibility exists that a clinical case of rubella in a pregnant female is attributable to the administration of rubella vaccine.

Blood samples for viral serologic tests, other than rubella HAI, should be sent to the Public Health Laboratory in the newly designed round, styrofoam virus shipper which will be available for distribution by June 1, 1970. In addition to containing six vacutainer tubes for

*Supervisor, Virus Diagnostic Section Public Health Laboratory.

serology, other than rubella HAI, the large styrofoam mailer is equipped with two virus swab outfits for throat or rectal swabs, one sterile empty vial for stool and autopsy specimens plus an appropriate form which is wrapped around each specimen container. Unless indicated otherwise, tyrpticase soy broth is used where transport medium is indicated.

The acute phase serum for serology tests should be collected as soon as the nature of the illness is suspected; the convalescent phase serum should be drawn 2-4 weeks after the first sample is obtained. If possible, it is preferred that the samples reach the laboratory as 5 ml aliquots of uncontaminated sera (or 6-8 ml whole blood.) The acute phase sample may be sent to the laboratory soon after it is collected, or if preferred, the serum (not the whole blood) may be frozen for subsequent shipment with the convalescent phase sample. Paired sera are requisite to demonstration of a significant increase in antibody titer. A four-fold or greater rise in titer between the acute and convalescent sera usually signifies current infection.

Materials to be submitted to the laboratory for viral isolations should be collected aseptically in the acute phase of illness, preferably while the patient is febrile. Viral isolations are facilitated if specimens are frozen immediately after collection and if the frozen state is maintained throughout the storage and transit periods. Just prior to shipment of specimens for isolation of virus, the #303 can containing water should be frozen solidly and replaced in the space provided for it in the center of the shipper. The general rule for freezing of speciments for viral isolation pertain to all specimens except those suspected of harboring Respiratory Synctial Virus (RSV) or Cytomegalovirus (CMV). The thermolability of both RSV and CMV dictate that suspect specimens be inoculated directly into tissue culture within 2-4 hours after collection and the freezing of such specimens be avoided. If delays in isolating RSV and/or CMV are unavoidable, it is preferable to store samples at 4°C.

If an illness is one caused by a single specific virus (e.g., measles, mumps, or rubella) recovery of the virus constitutes confirmation of the etiology of the current illness. When considering enteroviruses or viruses commonly associated with respiratory disease syndromes, the problem of specific etiologic agent is necessarily complex. Many viruses are widely distributed in communities causing subclinical infections, minor illnesses as well as overt disease. It is important to realize that in such a situation the isolation of a virus (even if accompanied by a measurable increase in specific antibody) does not arbitrarily indicate that the isolated agent caused the patient's current illness. Isolation from pleural or pericardial effusions, from cerebrospinal fluids, urine, or blood help to substantiate the probability of a viral etiologic association, but caution should be the rule in evaluating the importance of a virus isolated solely from the throat or feces, particularly in sporadic cases.

The value of an etiologic diagnosis of a viral disease is frequently challenged by the physician because the patient with uncomplicated viral disease usually recovers before the etiologic agent can be identified. It is true that such information infrequently guides the clinician in his choice of therapy; however, it should be remembered that diagnostic virology is currently at the stage in development that diagnostic bacteriology reached a half century ago. Refinements in techniques of isolation and identification of viruses are developing rapidly and soon answers will be available to clinicians in hours rather than the traditional lapse of weeks or even months. Soon there should be specific effective forms of therapy and prophylaxis available for viral diseases. Despite the present paucity of therapy, etiologic diagnosis of viral infections provides benefits for the clinician beyond the satisfaction of knowing what virus caused the patient's illness. An immeasurable epidemiologic dividend of viral diagnostic efforts is knowledge of the viral agents prevalent in the communities of Maine which ultimately aid in suggesting possible clinical diagnoses. Effective utilization of available virus diagnostic facilities and services serve to increase the awareness of clinicians of the specific viruses responsible for the greatest percentage of acute infections in the State of Maine. In time, the result should be sharpened awareness in differentiating illness due to viral and bacterial agents. It has been suggested[2] that this tends, in turn, to diminish unwarranted use of antibiotics thereby minimizing drug reactions and drug sensitization in patients with viral diseases.

One of the major roles of a progressive virus diagnostic laboratory is to explore and develop techniques which will enable the clinician to obtain viral diagnoses in the shortest possible time. A continuing effort will be made by the staff of the virus diagnostic facility in the State of Maine to develop and utilize the most expedient methodologies for virus diagnostic work.

In the immediate future, all physicians and hospital laboratory directors, currently registered in the State of Maine, will receive a brochure prepared by the staff of the Diagnostic Virology Section. The brochure describes in detail the services available for Viral and Rickettsial diseases. It is hoped that by August 1, 1970 the local facility will be ready for accelerated viral diagnostic services.

References

1. Hermann, K. (NCDC, Atlanta, Ga.) Personal Communication – April, 1970.
2. Horstmann, D. M. 1965, Clinical Virology, A.J.M. 38: 651-668.

AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

Grants for Cancer Research Announced

Isaac M. Webber, M.D., Chairman Research Committee (left), presents grants to Doctors Johnston and Carroll

Grants totaling $99,247.50 for cancer research, at Jackson Memorial Laboratory, Bar Harbor; University of Maine, and Maine Medical Center in Portland, have been announced by Miss Fran Hapgood of Portland, 1970 Maine Cancer Crusade Chairman.

"These grants for research," Miss Hapgood said, "cover a wide variety of studies aimed at opening the door to the secret of the dread disease that will strike one of every four families in 1970."

Doctor Earl L. Green of the Jackson Memorial Laboratory has been given a grant of $24,000.00 as a special bequest from the Janice M. Blood estate, to support the study of "The Genetics of the Mouse."

Dr. Elizabeth S. Russell, also of Jackson Memorial Laboratory, has been given a grant of $33,175.00 for a study of "The Action of Lethal and Other Deleterious Genes Affecting Growth and Differentiation." This grant is known as the Janice M. Blood Memorial Grant for Cancer Research from the American Cancer Society.

Doctor Edwin D. Murphy of Jackson Memorial Laboratory has been awarded a grant of $15,000.00 for a study of "The Exploitation of Tumor-Specific Antigens in the Therapy of Hodgkin's-Like Tumors of Strain STL/J Mice."

At Maine Medical Center in Portland, Doctors Hugh H. Johnston, Director of Endocrine Research Laboratory, and Ronald Carroll, Director, Division of Oncology, will study together, "Circadian Rhythms of Estradiol in Humans with Benign Breast Tumors, Carcinoma of the Breast, and Adenocarcinoma of the Endometrium." $11,822.50 has been granted for this all-important study.

An additional $12,500.00 has been granted Doctor Johnston for a study of "The Effect of Estradoil Antibodies on Estrogen-Dependent Mammary Tumors."

In making the announcement, Fran Hapgood pointed out, "every citizen of Maine is entitled to know just where the dollars donated to the Cancer Crusade go, and that," she continued, "is the sole purpose of this report."

"Doctor Murphy's grant at Jackson Memorial Laboratory, and those to Doctors Hugh H. Johnston and Ronald Carroll at Maine Medical Center are funds from the Florence M. Kerrison Memorial Grant for Cancer Research in Maine, as is the grant to Julian F. Haynes at University of Maine, Orono.

Julian F. Haynes, Associate Professor of Zoology at the University of Maine, Orono, has been given a grant of $2,750.00 for studies on Scarlet-Red Induced Tumors in Hydrozoan Polyps."

"During the past decade," Miss Hapgood said, "more than one million dollars in cancer research grants have been given to the famed Jackson Laboratory and the University of Maine."

"Continued research, plus increased public education to bring about an awareness of the seven warning signals of Cancer are the tools that will save millions of lives in the days to come," Miss Hapgood said. "The real life-saver," she went on to say, "is in the annual checkup which will bring about early awareness of cancer, and one of every two stricken will be saved."

Honorary Pin Recipients Receive Awards at 1970 Annual Session of the M.M.A.

Presentation of the Association's Honorary Pins were made by Charles F. Branch, M.D., President of the M.M.A., at the Annual Banquet, Monday evening, June 8 at 7:00 P.M.

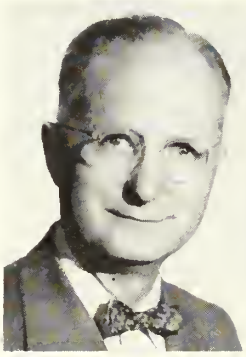
FIFTY-YEAR PINS

Fifty-Year Lapel Pins were presented to the following members who were graduated from Medical School in 1920:

Cumberland County

WINIFRED W. CURTIS, M.D. – Dr. Curtis, who now resides at Bailey Island, Maine, is a native of Brooklyn, New York. She was graduated from Vassar College in 1915, attended Cornell University Medical College from 1915 to 1917 and received her medical degree from Boston University School of Medicine in 1920. Dr. Curtis took postgraduate courses at Long Island College Hospital and Kings County Hospital in Brooklyn, New York, and at the University of Colorado, Denver, Colorado. She had hospital appointments at Mather Memorial Hospital and St. Charles Hospital in Port Jefferson, New York and practiced in Stony Brook, Long Island, New York before coming to Maine in 1968.

Dr. Curtis



Dr. Webber

ISAAC M. WEBBER, M.D. – Dr. Webber was graduated from Bowdoin College in 1917, Bowdoin Medical School in 1920 and in 1957 received an Honorary Degree of Doctor of Science from that institution. He interned at Worcester City Hospital, Worcester, Massachusetts and served residencies at the Mayo Clinic and the University of Minnesota. Dr. Webber was Chief of the Surgical Service at the Maine Medical Center from 1947 to 1957 and served as President of the staff from 1954 to 1956. He was Assistant Chief of Staff at the Mercy Hospital from 1954 to 1955. A specialist in Surgery, Dr. Webber has practiced in Portland since 1927. During World War II, he served on Portland's Board of Appeals for Selective Service. He is a native of South China, Maine.

Kennebec County

BLYNN O. GOODRICH, M.D. – Dr. Goodrich, a native of Skowhegan, Maine, is a general practitioner and has been located in Waterville since 1921. He received his medical degree from McGill University Faculty of Medicine in 1920, interned at Montreal General Hospital and served residencies at Montreal Maternity Hospital and at Grace Hospital in Detroit, Michigan. Dr. Goodrich served during World War I from March to December 17, 1918 and was discharged as a 1st Lieutenant in the Medical Corps.

Dr. Goodrich

Dr. Langer

ELLA LANGER, M.D. – A native of Vienna, Austria, Dr. Langer is now located in Augusta, Maine, where she was associated with the Department of Health and Welfare from 1945 to 1965 as Director of the Division of Maternal and Child Health and Crippled Children's Services. Since 1967, she has been Pediatric Consultant for Head Start and is on the staff of the American Academy of Pediatrics. Dr. Langer was graduated from the University of Vienna Medical College in 1920 and was an intern and resident at the University Clinic of Children in Vienna from 1920 to 1923. Since coming to the United States, she has served as visiting lecturer at Harvard University School of Public Health and as Research Fellow at Johns Hopkins University.

Knox County

GEORGE W. LOEWENSTEIN, M.D. – Dr. Loewenstein, a native of Germany, has been a citizen of the United States since 1945. He is a graduate of Friedrich Wilhelms University, Germany in 1920 and interned at the Berlin University Clinic. Dr. Loewenstein practiced in Chicago from 1941 to 1947 before coming to Maine, where he has practiced in Chebeague Island from 1947 to 1952 and in Islesboro from 1952 to 1958. Since 1958, he has been located in Clearwater, Florida and is Medical Consultant for the German Consulate, Atlanta, Georgia for North and Central Florida. He has written many papers about Preventive Medicine.

Oxford County

JAMES A. MACDOUGALL, M.D. – Dr. MacDougall was President of the Maine Medical Association in 1961-1962, President-elect in 1961 and Council Chairman in 1960-1961 and, prior to that, had served two terms as Councilor for the Second District. He received his medical degree from McGill University in 1920, interned at the Royal Victoria Hospital and was a resident at Montreal General and Children's Memorial Hospital. Dr. MacDougall took postgraduate courses at the New England

Dr. Loewenstein

Dr. MacDougall

Dr. Blaisdell

Dr. Thaxter

Medical Center. He is a general practitioner and practiced in Vermillion, Alberta, Canada from 1920 to 1923 before locating in Rumford where he is still in active practice.

FIFTY-FIVE-YEAR PINS

Fifty-Five-Year Pins were presented to the following members who received Fifty-Year Pins in 1965:

Cumberland County

ELTON R. BLAISDELL, M.D. – Dr. Blaisdell, a native of Westfield, Maine, was graduated from Bowdoin Medical School in 1915 and received an Honorary Degree of Doctor of Science from Bowdoin College in 1963. He was Director of the Diabetic Clinic at the Maine General Hospital from 1927 to 1937. Associate Chief Medical Service and Director of the Diabetic Clinic from 1937 to 1942 and from 1945 to 1947, and Chief of the Medical Service and Director of Diabetic Clinic from 1947 to 1956. From 1956 to the present time, he has served as Senior Consultant in Medicine at the Maine Medical Center. Dr. Blaisdell was located in Mapleton, Maine from 1916 to 1922 and has practiced in Portland from 1922 to the present time.

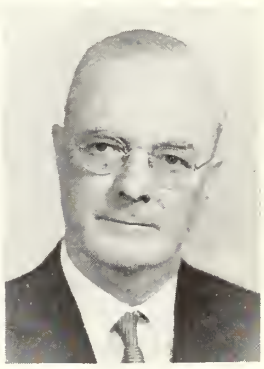
HORACE K. SOWLES, M.D. – Dr. Sowles received his medical degree from Harvard Medical School in 1915, interned at the Massachusetts General Hospital from 1915 to 1917 and served a residency there from 1917 to 1918. He was Visiting Surgeon at the Massachusetts General Hospital from 1920 to 1947 and Honorary Surgeon since 1947. He has also served as Chief of Staff and Consulting Surgeon at the Lawrence Memorial Hospital in Medford and as Consulting Surgeon at the Elliott Hospital, Keene, New Hampshire. He has been a member of the Courtesy Staff at the Maine Medical Center and Mercy Hospital since 1947. Dr. Sowles practiced Surgery in Boston from 1919 to 1947 and in Portland from 1947 to 1960 when he retired. He is a native of Barre, Vermont and now resides in Falmouth, Maine.

LANGDON T. THAXTER, M.D. – Dr. Thaxter, a native of Portland, Maine, was graduated from Harvard Medical School in 1915. He interned at the Massachusetts General Hospital from 1915 to 1916 and was a resident at Peter Bent Brigham Hospital from 1916 to 1917. From 1927 to 1928, he was a resident in Radiology at the Massachusetts General Hospital. Dr. Thaxter was a Radiologist at the Maine General Hospital and Maine Eye and Ear Infirmary from 1928 to 1954 and at the Marine Hospital in Portland from 1943 to 1945. From 1917 to 1919, he served with the U.S. Medical Corps and was discharged with the rank of Captain. Dr. Thaxter is retired and lives at Cumberland Foreside, Maine.

Kennebec County

ALBERT S. CRAWFORD, M.D. – Dr. Crawford was graduated from Cornell College of Medicine in 1915, interned at Lane Hospital in San Francisco from 1915 to 1916 and was a resident at New Haven General Hospital in Connecticut from 1916 to 1917. He took postgraduate courses at the Mayo Clinic and at Yale-in-China College of Medicine in China. He was Associate Professor of Surgery and Neurosurgeon at the University of Wisconsin from 1925 to 1926, Neurosurgeon at Henry Ford Hospital in Detroit from 1926 to 1952, at Thayer Hospital, Waterville from 1953 to 1955, and at the Veterans Administration Center in Togus from 1955 to 1963. Dr. Crawford was also associated with the Mt. Desert Hospital at Bar Harbor and at the Ellsworth General Hospital. He is now semi-retired and lives in Birmingham, Michigan.

Dr. Crawford



Dr. Woodcock

Penobscot County

ALLAN WOODCOCK, M.D. – Dr. Woodcock was President of the Maine Medical Association in 1959-1960 and President-elect in 1958-1959. He was Councilor for the Sixth District from 1955 to 1958, the latter year as Council Chairman. Dr. Woodcock was a graduate of Bowdoin Medical School in 1915, interned at the Eastern Maine General Hospital and was a resident at the New York Orthopedic Hospital from 1916 to 1917. He is an Orthopedic Surgeon and was on the staff of the Eastern Maine General Hospital and many other hospitals in the State. A native of Bangor, he is now retired and lives in that city.

York County

CHARLES W. KINGHORN, M.D. – A native of Yarmouth,

Dr. Kinghorn

Dr. Stevens

Dr. Devan

Dr. Russell

Maine, Dr. Kinghorn was graduated from Bowdoin Medical School in 1915 and interned at Worcester City Hospital in 1915 to 1916. He took postgraduate courses at the Chicago Eye, Ear, Nose and Throat Hospital from 1926 to 1930 and has practiced his specialty in EENT in Kittery since 1919. Prior to that, he practiced in Searsmont for one year. Dr. Kinghorn has served as Secretary-Treasurer of the York County Medical Society for thirty-eight years.

HAROLD W. STEVENS, M.D. – Dr. Stevens is a native of Saco, Maine. He was graduated from Harvard Medical School in 1914 and is a specialist in Preventive Medicine and Public Health. He interned at Massachusetts General Hospital and took postgraduate courses at Harvard School of Public Health. Dr. Stevens was on the staff at Tobey Hospital, Wareham, Massachusetts from 1945 to 1953 and was local Health Officer and State District Health Officer in Massachusetts from 1931 to 1953. He returned to Saco in 1953 and is at present acting as Physician Advisor for York County Head Start, York County Child and Family Guidance, York County Council on Aging, and State Advisory Committee on Aging.

SIXTY-YEAR PIN

A Sixty-Year Pin was presented to the following member who received his Fifty-Year Pin in 1960:

Penobscot County

THOMAS A. DEVAN, M.D. – Dr. Devan, a native of Brooklyn, New York, is now retired and lives in St. Petersburg, Florida. He was graduated from Johns Hopkins University Medical College in 1910, interned at Columbia-Presbyterian Medical College where he also served a residency. He was House Physician at the Peter Bent Brigham Hospital, Boston from 1919 to 1925. Dr. Devan has served as Professor of Hygiene at Rutgers, Assistant Director of Strong Memorial Hospital and Director of the Massachusetts General Hospital and the Eastern Maine General Hospital.

Dr. Pritham

SIXTY-FIVE-YEAR PINS

Sixty-Five-Year Pins were presented to the following members who received Fifty-Year Pins in 1955:

Androscoggin County

DANIEL F. D. RUSSELL, M.D. – Dr. Russell was born in Leeds, Maine and has practiced medicine there from 1906 to the present time. He received his medical degree from Bowdoin Medical School in 1905 and interned at the Central Maine General Hospital. Dr. Russell took postgraduate courses at the Pratt Clinic in Boston in 1919 and in 1921.

Piscataquis County

FREDERICK J. PRITHAM, M.D. – A native of Freeport, Maine, Dr. Pritham was graduated from Bowdoin Medical School in 1900. Dr. Pritham took a postgraduate course in Obstetrics at Tufts and has been Chief of Staff at the Greenville Hospital from 1912 to the present time. He has served as general practitioner in Greenville Junction and surrounding territory since 1906 and has written several interesting stories about his adventures in rural practice.

Schering

After only one year:

Administered to more people than live in Bangor, Lewiston, and Portland.*

Injectable Garamycin®
brand of
gentamicin sulfate injection

*An estimated 208,000 patients have received GARAMYCIN Injectable to date. The combined population of Bangor, Lewiston, and Portland is 144,500. (Estimated 1969 figures from The New York Times Encyclopedic Almanac 1970.)

See Clinical Considerations section on last page...

Mounting acceptance in the hospital...

Proven clinical effectiveness

Respiratory Infections

Outstanding results in serious gram-negative respiratory infections[1,2]

GARAMYCIN Injectable may prove successful where other antibiotics have failed.

Urinary Tract Infections

Strikingly effective in selected urinary tract infections[3]

With relatively low intramuscular doses, the promptly attained levels of GARAMYCIN achieved in the urine are considerably higher than the concentrations required for effectiveness against virtually all susceptible gram-negative pathogens. (Appropriate precautions are indicated in patients with impaired renal function; consult Package Insert for full details.)

Septicemia

May be lifesaving[4-6]

Numerous investigators have drawn attention to the value of GARAMYCIN Injectable in the treatment of gram-negative septicemias, often complicated by shock. Many hospital strains of *Serratia* are susceptible.[6]

Wounds and Burns

Response may be dramatic in wounds and burns complicated by sepsis[7]

The established efficacy of GARAMYCIN Injectable against *Pseudomonas*—as well as most other gram-negative pathogens—makes it an especially useful agent in the treatment of infected wounds and burns.

Important Precautionary Note Patients receiving treatment with GARAMYCIN Injectable (gentamicin sulfate injection) should be under close clinical observation because of the toxicity associated with the use of the drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with preexisting renal damage, treated with GARAMYCIN Injectable for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with preexisting renal damage.

This drug should be limited to the treatment of serious infections caused by susceptible gram-negative bacteria, with due regard for relative antibiotic toxicity. (See Clinical Considerations section.)

Mounting evidence in the laboratory...

Schering

Over 95% gram-negative pathogens sensitive*

No other antibiotic performed comparably *in vitro* against gram-negative pathogens.
In a nationwide culture audit of antibiotic sensitivity patterns, sensitivity reports from 106 hospitals, geographically representative by census tract and of varying sizes, were analyzed. During the three-month period, ***every*** gram-negative culture slip from ***every*** hospital was surveyed. The total number of cultures involved in the audit was 97,091. The total number of sensitivity determinations was 643,503.

Pathogens	Antibiotics* Percentage of sensitive strains / Number of strains tested							
	Garamycin	Kanamycin	Cephalothin	Cephaloridine	Ampicillin	Colistimethate	Chloramphenicol	Tetracycline
Klebsiella pneumoniae	99.5% 962	84.7% 992	86.2% 995	76.1% 67	32.7% 1,020	96.3% 640	82.9% 1,028	77.1% 1,026
Aerobacter aerogenes	95.9% 2,739	86.1% 2,818	53.5% 2,985	58.8% 1,514	22.7% 3,066	88.6% 2,603	85.8% 3,071	67.8% 2,981
Klebsiella aerobacter group	98.8% 566	83.9% 547	66.1% 522	60.5% 276	28.0% 553	89.5% 560	86.2% 587	62.8% 433
Klebsiella, all others	92.7% 2,944	83.3% 3,186	77.4% 2,976	67.5% 627	13.5% 2,883	95.0% 2,105	81.6% 3,212	70.6% 3,063
Pseudomonas aeruginosa	91.6% 4,528	29.8% 4,460	6.6% 4,418	6.6% 1,279	6.0% 4,360	91.3% 3,852	26.9% 4,608	26.4% 4,404
Proteus, indole-positive	91.8% 1,031	85.8% 1,062	39.9% 981	54.1% 364	40.2% 1,042	10.3% 758	76.1% 1,096	42.1% 1,051
Proteus mirabilis, indole-negative	94.9% 3,272	90.1% 3,378	83.1% 3,290	77.5% 975	78.0% 3,274	8.8% 2,634	85.9% 3,469	26.8% 3,278
Proteus, unspecified	96.2% 1,335	85.8% 1,371	71.7% 1,434	70.0% 647	64.7% 1,435	11.2% 1,233	76.0% 1,421	22.4% 1,298
Escherichia coli and all other *Escherichias*	96.4% 12,557	91.4% 12,818	87.8% 12,686	88.8% 4,251	74.6% 12,899	95.4% 10,623	94.1% 13,086	70.0% 12,559
Paracolobactrum, all	93.4% 303	88.9% 325	62.0% 305	74.2% 62	43.8% 340	80.9% 215	87.1% 350	72.6% 340
Coliform bacteria	99.0% 593	91.2% 649	81.5% 637	66.7% 21	52.7% 624	95.6% 607	91.6% 678	76.1% 637
Totals	95.1% 30,830	80.5% 31,606	65.3% 31,229	68.1% 10,083	50.3% 31,496	75.8% 25,829	79.7% 32,606	56.5% 31,070
Gram-positive (included for consistency with Package Insert, not an approved indication)								
Staph—*S. aureus*, coagulase-positive	97.4% 1,548	88.8% 1,458	97.7% 2,050	98.7% 636	61.1% 1,559	20.4% 628	94.4% 2,123	83.7% 1,966
Staph—*S. aureus*, unspecified	99.3% 993	92.8% 902	98.1% 1,289	95.3% 213	45.8% 1,153	29.3% 116	96.4% 1,427	82.3% 1,360

*Adapted from a three-month, nationwide hospital audit by R. A. Gosselin and Co., Inc., Dedham, Massachusetts (mid-May to mid-August, 1969).[8]
Antibiotics with significant gram-negative spectra are included. Organisms are listed as reported by laboratory.
Sensitivity testing was done by the disc method, a generally reliable test in the hospital setting. It should be noted, however, that the results with GARAMYCIN were somewhat higher than the results reported where the tube dilution technique was used. (See Clinical Considerations section which follows.) The concentration of the GARAMYCIN disc was 10 mcg.
Whereas standard testing methods were used by all hospitals, it is acknowledged that in a survey of this kind considerations such as differences in methodology are possible sources of error. The comparative percentage-sensitivity results derived from a survey of this kind are, therefore, not absolute. One should keep in mind also that the proper selection of an antibiotic is based not only on susceptibility testing but on relative toxicity and other clinical considerations as well.
It is felt, nonetheless, that the broad scope of the survey and the extreme care in data collection and tabulation permit a conclusion that the results are *generally* representative of current nationwide antibiotic sensitivity patterns.

Injectable Garamycin®
brand of **gentamicin sulfate injection**

See Clinical Considerations section on last page...

Injectable Garamycin®

brand of gentamicin sulfate injection

ADULT DOSAGE GUIDELINES

See definitive prescribing information in Package Insert.

Patients with Normal Renal Function

Total Daily Dose (administered in two, three, or four divided doses)			
Urinary Tract Infections (due to susceptible strains of gram-negative bacteria)†	**Less Severe** 0.8-1.2 mg./kg. for 7-10 days	**Resistant/ Moderately Severe** Larger doses or additional antibacterial therapy should be considered in severe urinary tract infections or in resistant cases involving the renal parenchyma or anatomic anomaly.	**Serious/Life-Threatening** up to 5 mg./kg.
Other Infections including bacteremia, infected surgical wounds, severe soft tissue infections, and respiratory tract infections (due to susceptible strains of gram-negative bacteria)	3 mg./kg. for 7-10 days		

†Alkalinization of the urine may be a useful therapeutic adjunct.

Patients with Impaired Renal Function

To minimize the risk of ototoxicity in patients with impaired kidney function, only the first dose should be that normally recommended. Each subsequent dose should be half or less of that recommended for patients with normal renal function, depending upon the degree of renal impairment.

In patients with renal failure who are undergoing 14-hour hemodialysis twice weekly, administration of 1 mg./kg. GARAMYCIN Injectable at the end of each dialysis period has been suggested.

Clinical Considerations

Indications: GARAMYCIN Injectable is clinically effective in infections due to susceptible strains of gram-negative bacteria, including *Pseudomonas aeruginosa*, and species of indole-positive and indole-negative *Proteus*, *Escherichia coli*, and *Klebsiella-Aerobacter*. Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose. If the susceptibility tests indicate that the causative organism is resistant to gentamicin sulfate, other appropriate antibiotic therapy should be instituted.

IN VITRO INHIBITION OF CLINICALLY IMPORTANT BACTERIA BY GENTAMICIN SULFATE (TUBE DILUTION STUDIES)

BACTERIA	No. of Strains Tested	No. of Strains (%) Inhibited by: 4 mcg./cc. or less		8 mcg./cc. or less*		No. of *In Vitro* Studies
Staphylococcus aureus	1,210	1,200	(99%)	1,206	(99%)	11
Pseudomonas aeruginosa	885	771	(87%)	828	(93%)	16
Escherichia coli	836	736	(88%)	779	(93%)	11
Indole-positive and indole-negative *Proteus* species	477	210	(44%)	358	(75%)	12
Klebsiella-Aerobacter species	292	205	(70%)	231	(79%)	10

*Number of strains (%) of gram-negative bacteria inhibited by 10 mcg./cc. or less are as follows: *Pseudomonas aeruginosa*, 828 (93%); *Escherichia coli*, 792 (95%); *Proteus* species, 393 (82%); *Klebsiella-Aerobacter* species, 284 (97%). From same studies as above.
Source: Package Insert

This drug should be limited to the treatment of serious infections caused by gram-negative bacteria, particularly *Pseudomonas aeruginosa*, *Proteus* and other susceptible organisms, with due regard for relative antibiotic toxicity. Therefore, the drug should be considered for use against gram-negative: 1. Bacteremia; 2. Infected surgical wounds; 3. Severe soft tissue infections, including burns complicated by sepsis; 4. Respiratory tract infections; and 5. Selected cases of urinary tract infection.

Contraindications: GARAMYCIN Injectable is contraindicated in individuals with a history of hypersensitivity or toxic reactions to gentamicin.

Schering

Warnings: Patients receiving treatment with GARAMYCIN should be under close clinical observation because of the toxicity associated with the use of this drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those wi pre-existing renal damage, treated with GARAMYCIN Injectabl usually for longer periods or with higher doses than recommende

GARAMYCIN Injectable is potentially nephrotoxic, and th should be kept in mind when it is used in patients with pre-existin renal impairment. Kidney function diminished by infection of th upper urinary tract may, however, improve during effective trea ment with GARAMYCIN Injectable.

Concurrent administration of potentially ototoxic drugs such streptomycin and kanamycin or of potentially nephrotoxic dru such as polymyxin, colistin, and kanamycin with gentamicin sulfa has not been shown to afford any clinical advantages and, moreov may result in additive toxicity. Monitoring of vestibular, cochlea and renal function will provide guidance for therapy in such case

Precautions: In patients with impaired renal function in whoi serious infection develops, serum concentrations of the drug ma rise, with consequently increased risk of ototoxicity. In these pa tients or in those in whom recommended dosage or duration c therapy must be exceeded as a life-saving measure, routine studie of kidney function should be performed when possible. These ma be supplemented by evaluation of the vestibular and auditory func tion and measurement of serum concentration of the drug whe feasible. Serum concentrations of gentamicin should be maintaine below the range of 10-12 mcg./ml. to reduce risk of ototoxicity.

Ordinarily, treatment should not be given for more than 7 to 1 days or be repeated unless required for serious infection not re sponsive to other agents.

As with other antibiotics, treatment with GARAMYCIN Injectabl may occasionally result in overgrowth of nonsensitive organisms. I superinfection occurs, appropriate therapy is indicated.

Safety for use in pregnancy or the potential for fetal ototoxicity o nephrotoxicity have not been established. Studies in pregnant ani mals have not revealed teratogenic or ototoxic effects in the fetus GARAMYCIN Injectable should not be used in pregnant patients o in women of childbearing age unless its use is deemed advisabl by the physician.

Adverse Reactions: The overall incidence of ototoxicity considere related to treatment with GARAMYCIN Injectable was 2.8 per cen (16 of 565 patients). Contributory factors (two or more factors wer relevant to most patients) were as follows: 10 had azotemia, 1 received a total of 1 gram or more of the drug, 7 had recently re ceived other potentially ototoxic antibiotics (streptomycin or kana mycin), and 5 were over 60 years of age. Six also had decrease high-tone hearing acuity, which returned to or toward normal i the 4 patients retested.

Analysis of BUN data indicated that 4 (2%) of 172 patients showe increases in BUN that were probably related to treatment wit GARAMYCIN Injectable. Of 20 increases probably or possibly relate to treatment, 7 were reversible, 9 occurred in terminal patients, an 4 had no follow-up.

Other adverse reactions associated with treatment were one instanc each of urticaria, decreased hematocrit, and reversible depression of granulocytes with normal bone marrow. Other rarely reported and possibly treatment-related adverse reactions were anemia, increased reticulocyte count, rash, purpura, drug fever, hypotension convulsions, twitching, salivation, nausea, vomiting, increased transaminase activity (SGOT or SGPT), increased serum bilirubin, decreased serum calcium, and joint pain.

Packaging: GARAMYCIN Injectable, 40 mg./cc., 2-cc. multiple-dose vials, for intramuscular administration.

References: (1) Brayton, R. G., and Louria, D. B.: Gentamicin in gram-negative urinary and pulmonary infections, Arch. Int. Med. *114*:205, 1964.* (2) Louria, D. B.; Young, L.; Armstrong, D., and Smith, J. K.: Gentamicin in the treatment of pulmonary infections, J. Infect. Dis. *119*:483, 1969. (3) Cox, C. E.: Gentamicin, a new aminoglycoside antibiotic: Clinical and laboratory studies in urinary tract infections, J. Infect. Dis. *119*:486, 1969. (4) Groll, E.: Clinical experience with gentamicin, data from 12 German clinics, in Gentamicin: First International Symposium, Paris, January 1967, Lucerne, Essex Chemie AG, pp. 121-128.* (5) Jackson, G. G.: Laboratory and clinical investigation of gentamicin, *ibid.*, pp. 62-74. (6) Medeiros, A. E.: Discussion, J. Infect. Dis. *119*:533, 1969. (7) Polk, H. Discussion, J. Infect. Dis. *119*:529, 1969. (8) Three-month, nationwide hospital audit by R. A. Gosselin and Co., Inc., Dedham, Massachusetts (mid-May to mid-August, 1969).

*Dosage in this investigational study was less than now recommended in Package Insert.

For more complete prescribing details, consult package insert or Physicians' Desk Reference. Schering literature is also available from your Schering Representative or Medical Services Department, Schering Corporation, Union, New Jersey 07083.

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Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Etiology and Pathogenesis of Hypertension

HARRIET P. DUSTAN, M.D.*

Hypertension is a major cardiovascular problem that is largely unsolved. However, there are a variety of drugs available for treatment which used singly or in combination reduce arterial pressure substantially. Such therapeutic effectiveness tends to obscure the fact that we actually know very little about the mechanisms of hypertension and the functional details of its natural history.

Hypertension is a symptom, not a disease. We know it to be associated with a variety of diseases, but these affect only a small number of patients so that in most hypertension is without apparent cause. This condition is called essential hypertension. The term is an archaic misnomer because we now know that hypertension is not essential for anything. Long gone are the days when physicians believed elevated arterial pressure to be essential for maintenance of tissue perfusion.

Although elevated blood pressure, of itself, is a symptom, it is often associated with vascular diseases — arteriolar sclerosis or premature atherosclerosis. Arteriolar disease occurs more commonly in patients with severe diastolic hypertension, while premature atherosclerosis is usually a manifestation of long sustained arterial pressure elevation, even one of mild degree.

Hypertension can be classified in a number of ways according to: 1) the type of arterial pressure elevation — systolic, diastolic, or mixed, 2) the character of the elevation — labile or sustained, 3) severity of the associated vascular disease — mild, moderate, severe, or malignant (accelerated), 4) or etiology — renal, adrenal, cardiovascular, or essential. At our present level of knowledge, the etiologic classification is the most interesting. Not only does recognition of the various causes of elevated arterial pressure lead to more rational treatment, but also it gives an opportunity to study the mechanisms of hypertension.

The hypertensions that are associated with various diseases are called secondary. When none of these conditions is present, the hypertension is said to be primary. This term, like "essential," is a misnomer because each hypertension has a cause even though our knowledge is not sufficient to recognize it. Clearly, the more we have learned the more we have seen; for example, consider the types of hypertension recognized in the past 20 years. These include primary aldosteronism, renal arterial disease, and increased activity of the beta-adrenergic component of the sympathetic nervous system. Before these types were recognized, such patients were considered to have "essential" or "primary" hypertension.

The physiologic abnormalities that have been found in hypertensives relate to the nervous control of the circulation, catecholamines, cardiac output and peripheral resistance, adrenal steroids, the renal pressor system and plasma volume. Evidence is accumulating that these factors do not operate alone, and it seems likely that they make up an integrated system, one expression of which is elevated blood pressure.

When considering the etiology and pathogenesis of hypertension, it is an interesting exercise to see how these various factors are interrelated in the different types of hypertension. Of course, our present information is incomplete, but enough is available to make the exercise worthwhile.

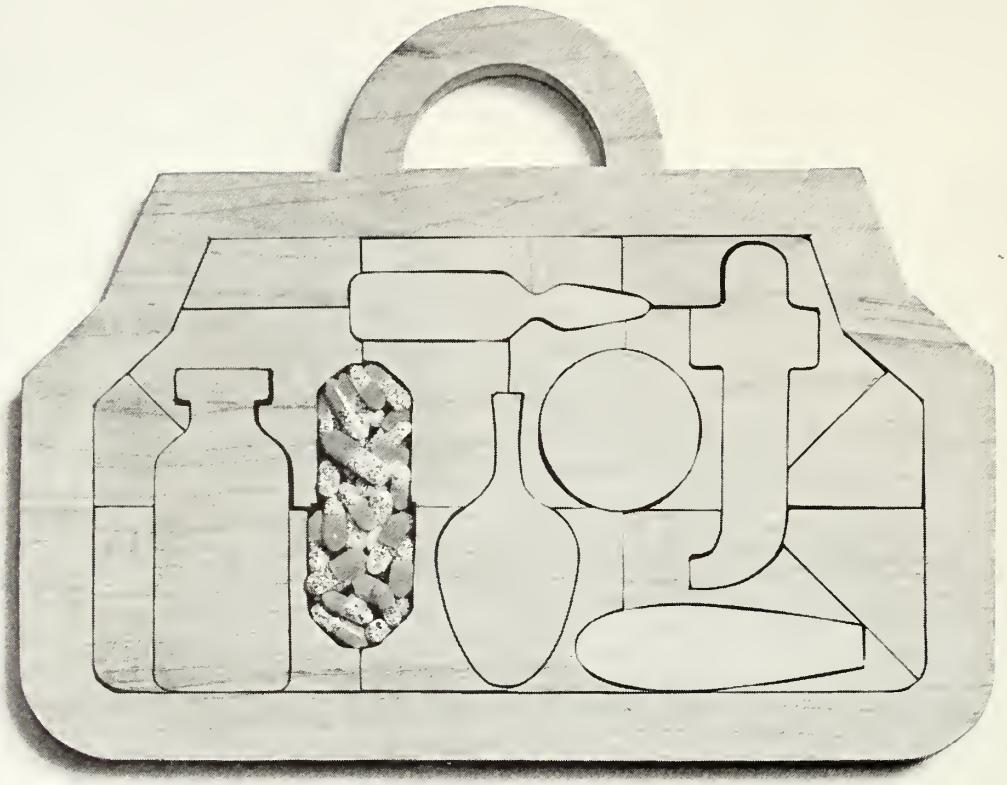
The most frequently occurring secondary hypertensions now recognized are those associated with renal arterial disease and renal parenchymal disease, pheochromocytoma, primary aldosteronism, coarctation of the aorta and increased activity of the beta-adrenergic nervous system.

In patients with renal arterial disease, the most likely cause of hypertension is, of course, the renin-angiotensin system. However, elevations of renin (which is the component most readily measured) are not routinely found. This suggests that other factors are also operating and since blood pressure can be lowered with drugs that suppress the activity of the sympathetic nervous system, this indicates a nervous component in the hypertension as well. In fact, we have recently shown that these patients often have exaggerated increases in blood pressure in response to head-up tilt. Further they tend to have slightly increased cardiac output which may represent an increase in nervous stimulation of the heart. Plasma volume can be decreased and, in our experience, it is inversely related to the plasma renin activity. Additionally, aldosterone production is often increased producing a state of secondary aldosteronism. Thus, although we cannot put together all the pieces of information in an integrated fashion, evidence is accumulating that the hypertension accompanying renal arterial disease is an expression of a variety of abnormalities, only one of which is a disturbance of the renin-angiotensin system.

In renal parenchymal disease, there is not so much

Continued on Page 134

*Research Division, Cleveland Clinic, Cleveland, Ohio.
Prepared by the Maine Heart Association for this Journal.



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Across The Desk

Local Comprehensive Health Services

Sen. Javits (R) N.Y. introduced S. 3830, the Local Comprehensive Health Service Systems Act of 1970, commenting that his bill was essential if we are to head towards a national health insurance scheme. . . . The Javits' bill authorizes the Secretary of HEW to make loans and grants, and provide technical assistance, to organizations to plan and develop local comprehensive health care programs and to aid them in becoming self-supporting (emphasis on programs in ghetto or disadvantaged areas). It also establishes criteria for the local systems which are seeking governmental assistance, requiring that they develop preventive health care programs, train and employ allied health personnel, and be organized in such a way as to be consistent with the States' overall comprehensive health care plan. The local programs would have to emphasize local consumer and community involvement in the planning, development, and operation of the comprehensive health services systems.

The proposal authorizes the Secretary of HEW to make grants to hospitals, medical schools, insurance carriers, non-profit private plans, and non-profit community groups to *pay 80% of the cost of planning and developing the comprehensive health services systems. It also authorizes the Secretary of HEW to pay that portion of the administrative, operating and maintenance costs of approved programs which exceed their income during the first five years of operation.* The bill defines a comprehensive health service system as one which is providing health care to an identified population group in a primary service area on the basis of contractual arrangements which embody a group practice established by a medical school, hospital medical staff, medical center, or other entity among the participating providers of services. It defines a "comprehensive health service program" as one which offers at least all the services provided under Parts A and B of Medicare, and must include annual physical checkups, the provision of maintenance prescription drugs, and dental services for children under 8 years of age. The Secretary of HEW could require other appropriate preventive and comprehensive health care services.

Senator Javits, after outlining his bill, commented, "It is vital to proceed immediately with the rationalization of medical care services and facilities if we are going to be able to establish some plan, even if it is the plan of the American Medical Association, for national health insurance." . . . The Javits' bill has been referred to the Senate Labor and Public Welfare Committee. – *Legislative Roundup, Vol. XI – LR 16, May 15, 1970*

Increase in A.M.A. Dues Recommended

AMA'S BOARD OF TRUSTEES, at its meeting in Washington, D.C., voted to recommend an increase of $80 in AMA membership dues, effective Jan. 1, 1971. The recommendation, which would raise the cost of a physician's membership from $70 to $150 per year, will be submitted to the House of Delegates at the Annual Convention, June 21-25, in Chicago. The last dues increase was in 1967. Noting that the Association is operating at a deficit this year and that inflation has caused a rise of more than $4.5 million in expenditures since 1967, the Board said a dues increase is needed to 1) operate new and expanded programs, without which the AMA cannot provide leadership in health affairs; 2) provide for federal taxes on "unrelated business income"; 3) maintain the AMA's reserves as directed by the House of Delegates; 4) provide for rising operating costs in an inflationary economy. A background paper describing the financial situation and some of the programs demanding priority attention will be included in the House of Delegates Handbook, which is scheduled for mailing on May 25.

THE BOARD ALSO will recommend that the House of Delegates change the AMA policy on abortion. Present policy opposes induced abortion

except for therapeutic reasons and under certain conditions. The Board points out that in recent months several states have amended their laws to permit abortion for reasons other than therapeutic, with the result that many physicians find themselves unable to perform a legalized medical procedure without violating AMA policy. The Board proposes that policy be revised to permit the decision to interrupt pregnancy to be made by the woman and her physician, but that no physician be required to perform an abortion and that no hospital be required to admit a patient for abortion.

THE BOARD VOTED to proceed with the development of a national professional liability insurance program for AMA members. The Board's Committee on Professional Liability reported that its proposal for such a program would provide for joint sponsorship by the AMA and state medical associations. The AMA program would not compete with programs presently established by medical societies. Further details will be worked out at a meeting of the committee on June 7. A National Congress on Patient Safety, jointly sponsored by the AMA and the AHA, will be held in 1971. Establishment of a continuing Committee on Professional Liability was approved by the Board. The committee will be composed of three trustees and two members of the House.

THE POSITIVE SIDE of health care in America will be presented in two half-hour television programs. The Board of Trustees approved development of the two programs which will be produced and distributed by the AMA to 200 TV stations. These programs, the Board stressed, will not be in reaction to the recent negative CBS programs, but will present to the public the many constructive efforts being made by physicians and others to solve the nation's health care problems. – *AMA Newsletter, Vol. 2, No. 20. May 18, 1970*

Briefly in the News:

–Another task force, sponsored by the *Association of American Medical Colleges,* has proposed a plan for admitting greater numbers of qualified minority students to medical schools. The report recommends in detail how medical schools can increase enrollment of minority students from the present 2.8 percent of the total to 12 percent by 1975-76. – *Washington Report on Medicine & Health, No. 1194, May 18, 1970*

–The Internal Revenue Service has ruled that *Medicare fees earned by staff physicians* of a hospital but collected and used by an exempt organization are includible in the physician's gross income. However, the doctor can deduct the amounts as charitable contributions. The ruling is found in the "Internal Revenue Bulletin" for April 13. – *Washington Report on Medicine & Health, No. 1192, May 4, 1970*

TRAINING OF NON-PHYSICIAN associates is the keystone toward much needed improvement in the methods of delivering health care to women, President-Elect J. Robert Willson, MD, told members of the American College of Obstetricians and Gynecology in his inaugural address at the 18th annual clinical meeting in New York. Such associates can relieve the busy obstetrician-gynecologist of many tasks, Dr. Willson said. As examples, he cited the potential usefulness of "intellectually competent" associates in prenatal education, counseling on contraception and family planning and sharing in the supervision of care during the prenatal period, during labor and in the postpartum period. "Properly trained non-physician associates can perform periodic breast and pelvic examinations, fit diaphragms, insert intrauterine contraceptive devices and do many things which require principally the development of manual skills," he said. Dr. Willson, a member of the U. of Michigan staff, said it is unfortunate that "misunderstanding concerning the role of such professionals has led to unjustified rejection of the concept" by many physicians. He said they should not be viewed as potential rivals. – *AMA Newsletter, Vol. 2, No. 20, May 18, 1970*

County Society Notes

ANDROSCOGGIN

The meeting of the Androscoggin County Medical Association was held at the Central Maine General Hospital in Lewiston, Maine on March 17, 1970 with twenty-eight members present. The meeting was called to order by the President, Lionel R. Tardif, M.D.

The speaker of the evening, Dr. Dwight E. Harken, Professor of Thoracic and Cardiac Surgery at Harvard Medical School and Chief of Services at Peter Bent Brigham Hospital, was introduced by Charles W. Steele, M.D.

A short historical review of cardiac surgery was presented. His talk on two conditions: aneurysm of heart wall, and areas of irritable foci (arrhythmias) was documentated by a color film showing corrective operative procedures. His address was followed by a question and answer period.

Waldo A. Clapp, M.D. read the resolutions of the death of William V. Cox, M.D. It was voted to inscribe our records with a copy, send a copy to the family and to the Maine Medical Association.

A letter was read from the Maine Medical Association stating that figures are not available on the number of persons not receiving adequate medical care in Maine.

There was some discussion on the rise of malpractice fees after reading the number of cases tried in the State last year and the amount of money paid for settlement or judgment.

It was voted that the May meeting would be at Lost Valley.

A letter was read from the County Bar Association urging that a medico-legal committee be formed (appointed) to work with the Lawyers Committee and the President appoint the Committee.

The Androscoggin County Medical Association met at St. Mary's General Hospital in Lewiston, Maine on April 16, 1970 with twelve members present. The meeting was called to order by the President, Lionel R. Tardif, M.D.

The guest speaker of the evening was Mr. Jack Simmons, Attorney at Law and Chairman of the Medico-Legal Committee. Mr. Simmons discussed the functions of a Medico-Legal Committee.

DONALD L. ANDERSON, M.D., *Secretary*

WASHINGTON

A regular meeting of the Washington County Medical Society was held at the Down East Community Hospital in Machias, Maine on March 30, 1970 with nine members and guests present. The meeting was under the direction of the President, George B. Shaw, M.D.

A letter was read from Attorney Francis Brown stating that he hoped to start soon to set up a set of "bylaws" for the Washington County Regional Health Agency.

A communication from Eliot T. Stadler, M.D. was read on a health survey made by Dr. Bhopinder S. Bolaria. The survey was made over Washington and Hancock Counties. Dr. Bolaria will be invited to the May meeting.

Drs. Rowland B. French of Eastport and Hazen C. Mitchell of Calais were nominated to the Board of Censors.

There was a discussion on the resolution put forth by the Piscataquis County Medical Society in the regard to Osteopathy. This resolution is to be presented to the interim meeting of the House of Delegates. Our delegate was instructed to ask that the last paragraph be deleted from this resolution. The Society instructed our delegate to favor the resolution put forth by the Somerset County Medical Society.

Dr. Shaw then introduced John B. Truslow, M.D. of the Penobscot Valley Regional Health Society. Dr. Truslow stated that he had been asked to make a partial survey of the need for a comprehensive approach to the handicapped children of Washington County and Hancock County. It has been proposed that a central hospital be set up in the Ellsworth area in connection with the Maine Coast Hospital to handle this comprehensive care, to be under the direction of a director, to have various specialties, such as pediatricians, orthopedists, otologists, etc., plus various social workers to formulate the plans for setting this up. Dr. Truslow said that certain monies had been set aside by William E. Schumacher, M.D. to make studies of the feasibility of the plan. Dr. Truslow said that there was a marked re-duplication of many of the State and Federal services and that there was a need of a comprehensive approach.

John Kazutow, M.D. stated that the State Public Health Service was desirous of running Rubella Clinics in Washington County. It was the feeling of the members that they would run their own clinics.

KARL V. LARSON, M.D., *Secretary*

CUMBERLAND

A meeting of the Cumberland County Medical Society was held on March 19, 1970 at the Stage Coach Restaurant in South Portland, Maine. There were seventy-eight members and guests in attendance. Guests included Mr. Lawrence Chapman of Noyes & Chapman Insurance Company, Portland; Mr. John Cross of Hartford Insurance Company, Portland; Mr. Leon Roy and Mr. George Hazel of Hartford Insurance Company; and John P. Dow, M.D., Representative of the Maine Malpractice Insurance Committee.

Following the social hour and dinner, the program was introduced by George F. Sager, M.D., President. Mr. Lawrence Chapman served as moderator and introduced the panel of speakers. Mr. George Hazel spoke on rates and some comparisons among New Hampshire, Vermont and Maine Malpractice Insurance. Mr. Leon Roy spoke about the establishment of a medical jurisprudence committee in the State of New Hampshire, and their excellent results through the use of this committee. Mr. John Cross discussed the Claims Management in Portland, Maine. This program was followed by a question and answer period which stimulated a lively discussion. In general, it seemed to be that there was some communications gap in Maine amongst doctors.

The business meeting was called to order at 10:00 p.m. The minutes of the last meeting were dispensed with after the proper vote. Announcements were made of the next meeting to be held April 16 at the Crescent Beach Inn in Cape Elizabeth, Maine. The Pownal Hospital will be in charge of the program. An announcement was made of the meeting of the House of Delegates in Brunswick.

DOUGLAS R. HILL, M.D., *Secretary*

HANCOCK

A meeting of the Hancock County Medical Society was held at the Castine Community Hospital in Castine, Maine on April 8, 1970 with twelve members and nine guests present.

John B. Truslow, M.D. discussed problems of regional medicine in the Comprehensive Health Care Planning Agency of the Penobscot Valley from his position as Research Director.

Joseph T. DeGrinney, M.D., resident of the Maine Medical Center, was introduced by Wesley J. English, M.D. as a guest of the Mt. Dessert Island Hospital. Dr. DeGrinney announced interest of the House Officer Association of the Maine Medical Center in community needs for physicians. Residents of the various specialties would like to visit communities on invitation from doctors.

Drs. Bradley E. Brownlow and Eliot T. Stadler were appointed to a committee to meet with Dean H. Fisher, M.D. concerning the resolution adopted by the Society in March

at the ending of the Maternal and Infant Care Program in Hancock and Washington Counties. A committee member from Bar Harbor was to be invited. The committee is to meet with Dr. Fisher before May 15th.

Robert F. Russell, M.D. discussed the proposed budget of the Maine Medical Association, particularly the dues increase to $85.00 or $100.00. Dr. Stadler discussed the Interim Meeting of the House of Delegates on April 5th. Nomination of a Councilor from Hancock and Washington Counties is due for June. A move to congratulate Dr. Russell for his service as Council member for our Society because of his loyalty to that position and leadership in the interest of medicine was heartily adopted by the members.

Mr. Fred Howard of the Blue Shield office discussed retroactive nonpayment of Medicare fees when utilization reports could not substantiate a need and level of care in institutions throughout the State of Maine. Mr. Thomas Cathcart explained the Usual, Customary and Reasonable Fee concept for Blue Shield contract. A stimulating discussion followed.

BRADLEY E. BROWNLOW, M.D., *Secretary*

LINCOLN-SAGADAHOC

The Lincoln-Sagadahoc County Medical Society met at The Ledges in Wiscasset, Maine on April 21, 1970.

The meeting was called to order by the President, Arkadij Oceretko, M.D. The minutes of the last meeting were accepted as read.

Dr. Bostwick read a letter from the Pine Tree State 4-H Club Foundation asking for funds. The subject was tabled indefinitely by unanimous acquiescence of the members.

The speaker, Jacob Dana, M.D. of the Veterans Administration Center in Togus was introduced by Henry A. Hudson, M.D. Dr. Dana spoke on Pre-coronary care.

GEORGE W. BOSTWICK, M.D., *Secretary*

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MAINE HEART ASSOCIATION NOTES — *Continued from Page* 129

information available concerning the possible pressor factors. However, there have been studies in patients with chronic renal failure which show expansion of the extracellular fluid volumes and correction of hypertension when these excesses are corrected by dialysis. Further, there is a suggestion that with expanded plasma volume the nervous control of the circulation is lessened — possibly because it isn't so necessary when the blood volume is high. Plasma renin activity has not been consistently found to be elevated although increased activity of the renin-angiotensin system seems likely in patients whose hypertension remits following bilateral nephrectomy done in preparation for transplantation. Thus, in this type of hypertension, there are indications that, in one way or another, three pressor factors participate — renal pressor, neurogenic, and fluid volume.

Pheochromocytoma seems a much more straightforward problem than that presented by the other two types of hypertension. Currently, we know that there is increased epinephrine and norepinephrine production, and this seems reason enough for the hypertension. Plasma volume can also be reduced, and this is important because it may explain the hypotensive crises that often occur in these patients following surgical removal of the tumor.

In primary aldosteronism, there is an increased production of aldosterone which can cause increases in body sodium, extracellular fluid volume and plasma volume. Along with these increases, decreased activity of the sympathetic nervous system has been reported. Plasma renin activity is low suggesting that this is not a factor in the hypertension.

Increased activity of the beta-adrenergic component of the sympathetic nervous system can be associated with hypertension. These patients have palpitations and exaggerated tachycardia in response to a variety of normal stimuli, such as exercise. They have increased cardiac output but a normal or near normal peripheral resistance. Their hypertension can be controlled with beta-blocking drugs such as propranolol.

Coarctation of the aorta is also recognized as an occasional cause of hypertension. If patients are not in cardiac failure, apparently hemodynamic functions are normal, at least in the upper parts of the body above the coarctation. However, until flow beyond the coarctation can be measured reliably, hemodynamic characteristics of this type of hypertension cannot be determined. Other pressor mechanisms have not been studied in such patients.

Although most treatments of hypertension are empiric rather than based on specific pressor mechanisms, information is becoming increasingly available in various types of hypertension which bids well to describe a number of integrated circulatory disturbances, of which hypertension is one manifestation. These descriptions will provide rational, rather than empiric, treatment.

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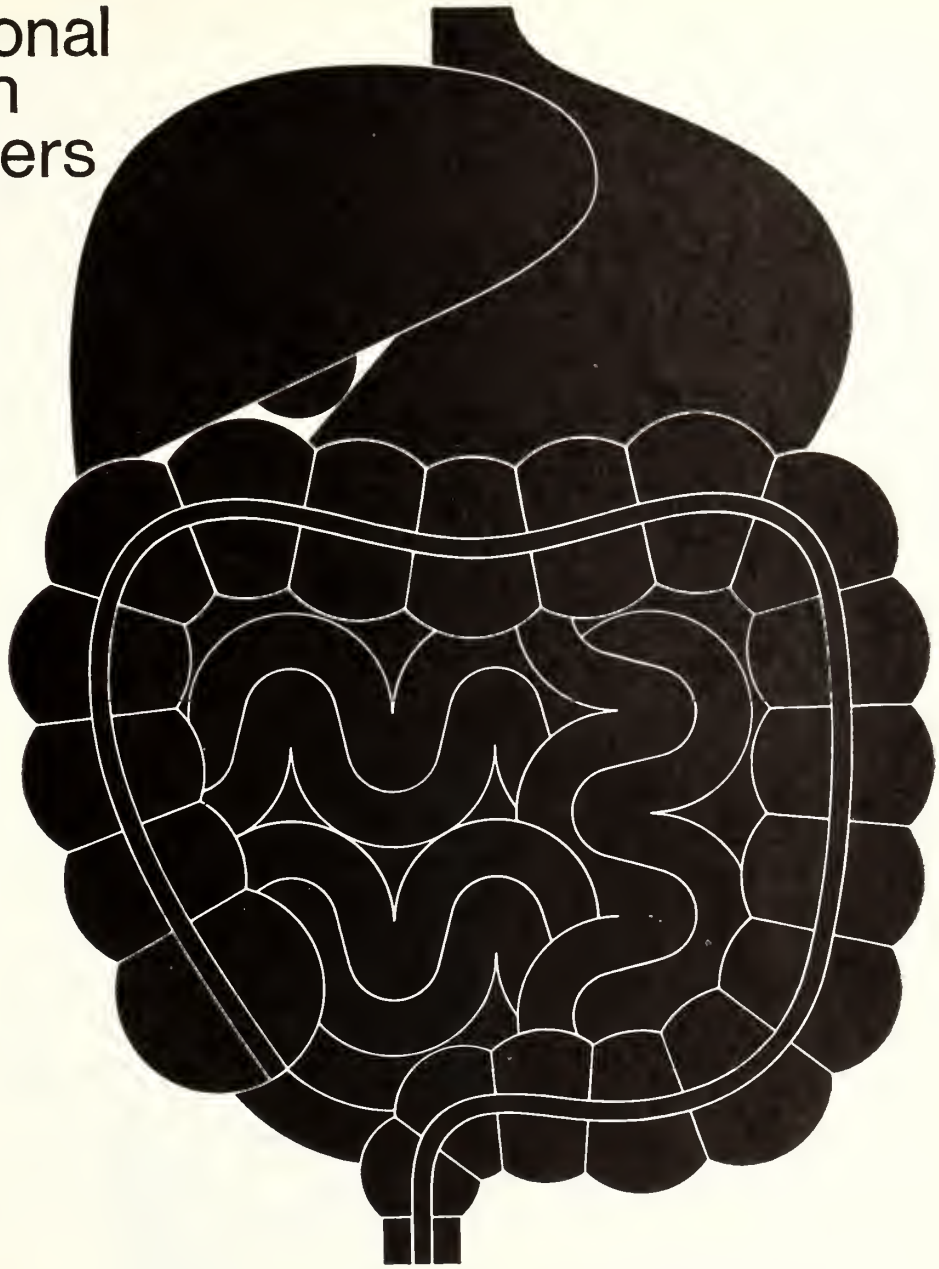

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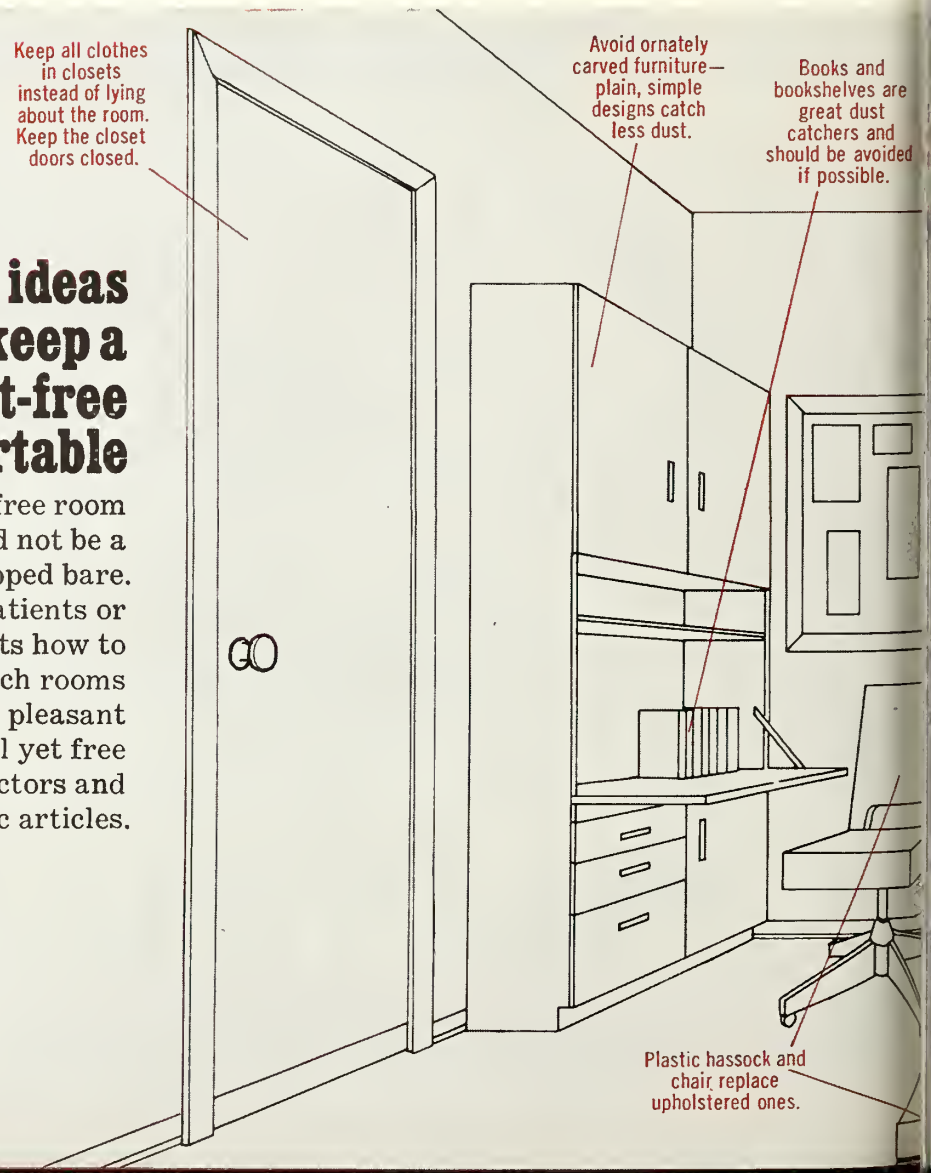

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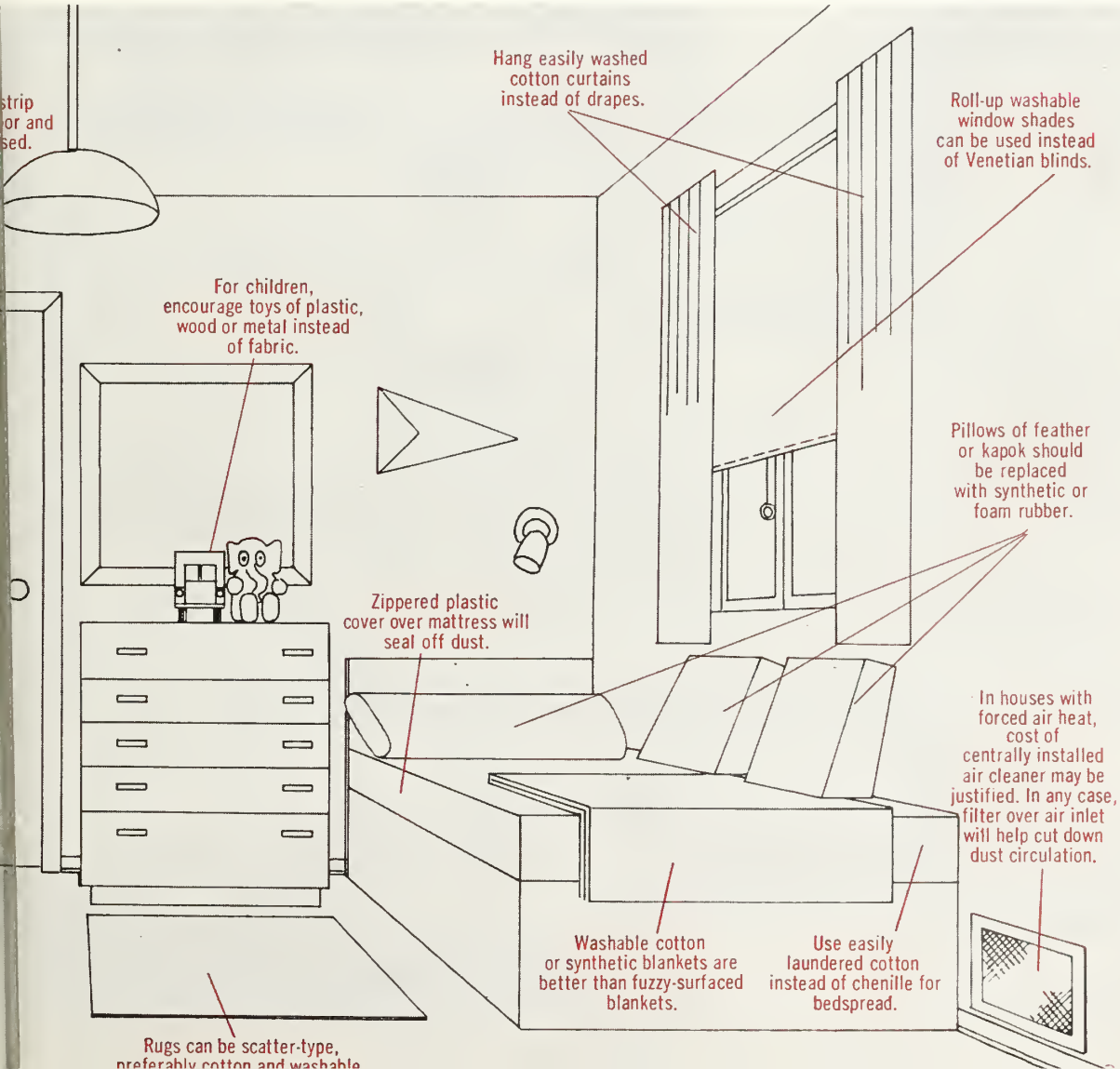

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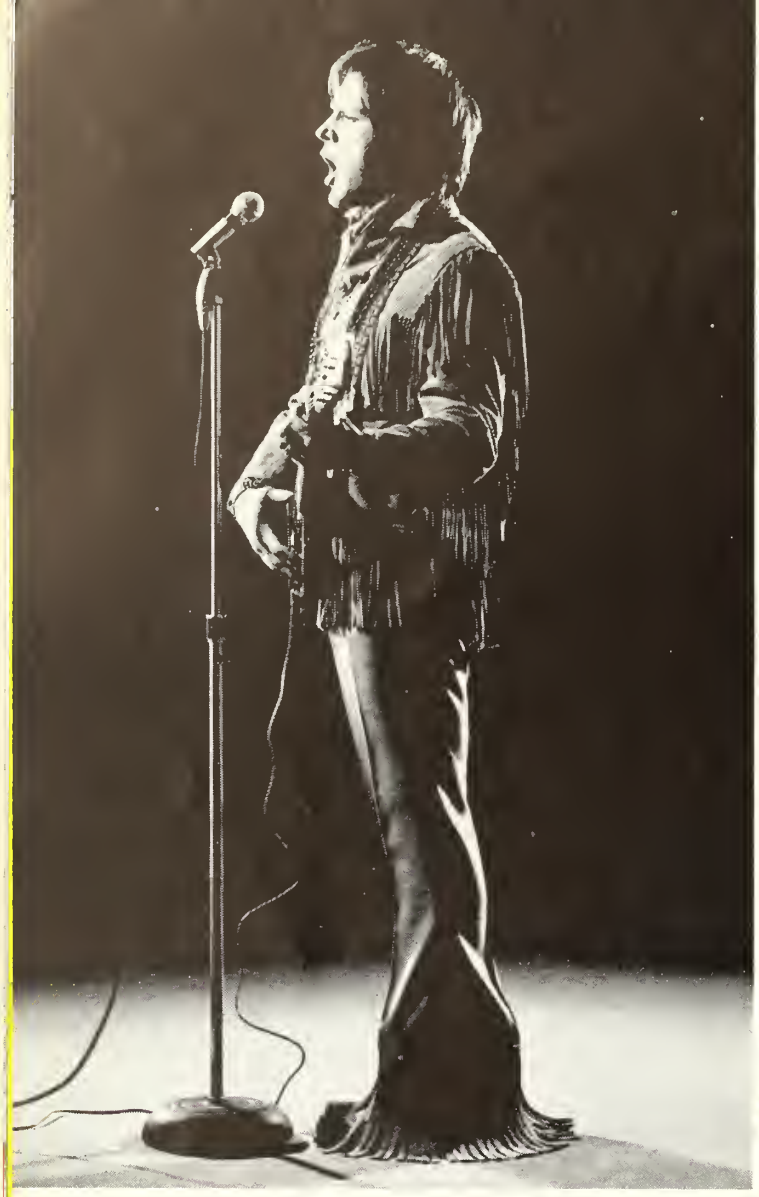

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The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

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Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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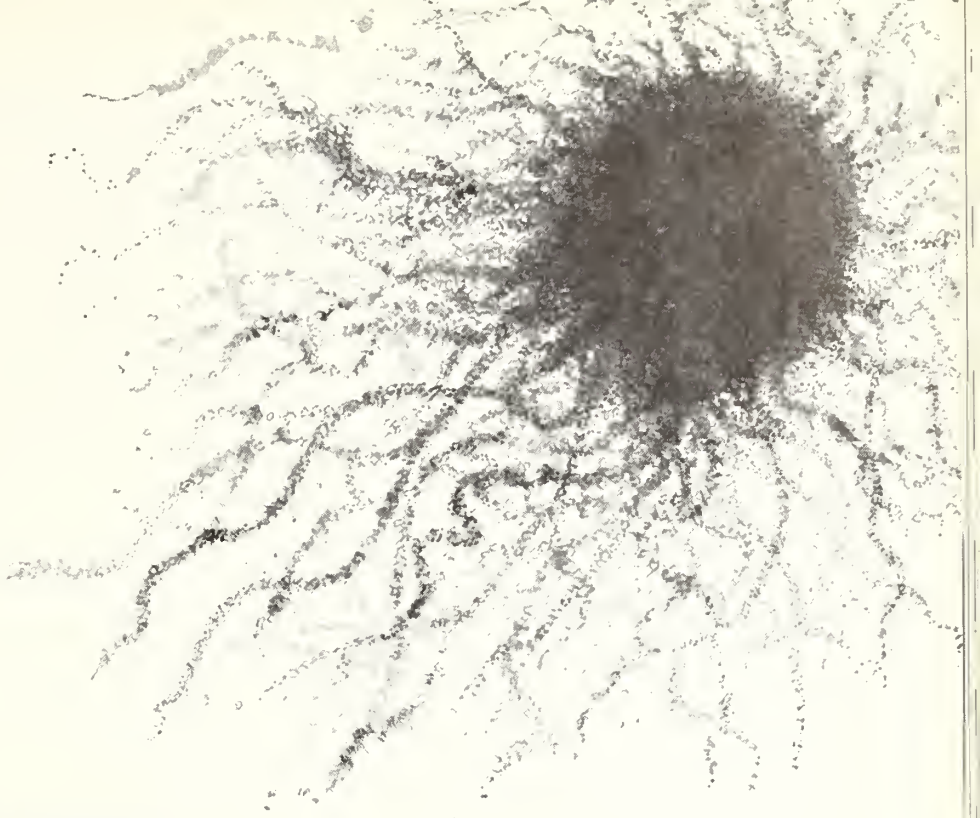

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North American Blastomycosis

The Second Reported Occurrence in Maine

ROBERT L. OHLER, M.D.*

The purpose of this paper is to report the second documented case of systemic North American blastomycosis occurring in Maine and to suggest that there may be an endemic focus of the disease in the northern part of the State. The other reported case, remarkably similar to this one,[1] responded to large doses of potassium iodide. At least two other cases, both unreported, are known to physicians in Maine.[2]

North American blastomycosis, a serious systemic fungus infection, was first described by Gilchrist in 1894. It originally was considered a skin disease. In 1939, a total of 347 cases had been reported. By 1951, the concept[3] that practically all cases were acquired by inhalation had become accepted generally. There are several excellent modern reviews of the disease and its treatment.[4,5,6]

ETIOLOGY

The organism Blastomyces dermatitidis is a single round or ovoid budding, thick-walled yeast-like organism existing also in a mycelial phase. A distinguishing characteristic is a wide region of communication between the parent and daughter cell. The organism grows easily on blood agar, beef infusion dextrose agar, or Sabouraud's glucose agar, the culture having a mold-like appearance at 37°C. and producing a filamentous growth at room temperature.[4]

EPIDEMIOLOGY

The organism has been isolated from the soil in Georgia[7] and has been found to persist and grow when inoculated into various soil samples. However, other attempts to isolate the organism from soil and other natural sources have failed. The majority of the cases have been reported in Southeastern United States, Midwest, and the South.[4] A few cases have been reported in Canada and the disease has been found recently in India and Africa, Mexico, and Central and South America. The disease must be distinguished from South American blastomycosis caused by a different organism, Blastomyces brasiliensis.

CLINICAL FEATURES

Contrary to the situation in the case of many other fungi, B. dermatitidis infects and invades healthy people. Males are affected more often than females. The disease is seen most commonly between the ages of 50 and 70 but it has been reported to involve patients of all ages including children.[8] An infection with this organism may co-exist with histoplasmosis and tuberculosis. In approximately two-thirds of the cases multiple organ systems are involved, skin and lung most commonly. Subcutaneous tissue abscesses are seen in 35 to 40% of the cases. The male G-U tract with prostatic abscesses and epididymo-orchitis, kidney, and female G-U tract less frequently are sites of infection. In 25% of the cases there is bone invasion, most commonly of the lumbar vertebrae, pelvis, skull, ribs and long bones, and osseous infection may extend into the adjoining soft tissue to form abscesses. Joint involvement is distinctly uncommon. X-ray appearance is that of osteolytic lesions. Oral and nasal mucous membranes, lymph nodes, liver, spleen, thyroid, larynx, the meninges, brain, extradural space, rarely the G-I tract, endocardium, appendix, tonsils, the uveal tract, cornea, nasal sinuses, and adrenals with the rare production of adrenal insufficiency all have been reported to be involved.[4,5]

Skin lesions occur in two varieties, the first being verrucous resembling cutaneous tuberculosis or cancer often with central healing and abscesses under the crust. These lesions are a good source of organisms when

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scrapings suspended in 10 or 15% potassium hydroxide are examined microscopically. The second type of skin lesion is a superficial ulcer resembling a mucous patch and this is also a good source of organisms. Subcutaneous abscesses are seen in a third of the cases.

Abernathy[9] from a study of 27 cases with pulmonary involvement found that no specifically diagnostic clinical pattern could be established. An infiltrative or fibrotic reaction was most common often with pleural reaction and thoracic adenopathy. Cavities, miliary lesions, pneumonia, and lesions radiologically resembling bronchogenic carcinoma were seen less frequently

Nonspecific constitutional symptoms of fever, malaise, and weight loss are common; erythrocyte sedimentation rate is elevated in two thirds; anemia is seen in 25%, leukocytosis in 25%, and nonspecific elevation of serum globulins in 70%.[5]

Diagnosis preferably is made by culture. The organism grows in 10 to 14 days at room temperature. The best sources are skin, sputum, pus from abscesses, and sometimes urine after prostatic massage. Isolation of the organism from the stool has been reported as have positive blood cultures on rare occasions. The organism has a characteristic appearance on histologic sections and especially on direct microscopic examination of material from a lesion.

The immunology of the disease has been studied extensively.[10] It has been said that the extent and severity of the disease and a poor prognosis are related to a high complement fixation titer and that a negative blastomycin skin test also indicates a poor prognosis. However, recent studies[5] found in a series of 40 patients that 28 reacted to histoplasmin and none to blastomycin. Stead[11] has emphasized recently that the currently available skin test material is unreliable and tests are rarely positive. It never should be relied upon for diagnostic purposes. The National Communicable Disease Center currently uses an agar gel diffusion test.

Natural History of the Disease

Systemic blastomycosis usually has an insidious onset and often is a slowly progressive disease, the course being measured in years. Lockwood, et al,[12] reported a series of cases with the duration of symptoms varying from two weeks to eight years. Occasionally it is rapidly progressive[8] and can resemble the severely progressive primary infection seen in other granulomatous diseases such as tuberculosis, coccidioidomycosis, histoplasmosis, and maduromycosis.[11] The ultimate fatality rate was 80% before stilbamidine and amphotericin became available but in two recent series it has varied between 8 and 13%. Relapses are not uncommon.

Therapy

Amphotericin B and 2-hydroxystilbamidine are both effective in arresting infection with B. dermatitidis in the large majority of cases.[13] Potassium iodide, the principal agent employed before 1950, occasionally was strikingly successful.[1,4] Roentgen therapy, previously used, no longer is recommended.[4]

The role of pulmonary resectional therapy is uncertain. Harrell and Curtis[4] believe it may have a place in the treatment of cavitary disease and is probably safe if covered by effective chemotherapy.

There is some difference of opinion concerning which of the two effective therapeutic agents should be used routinely.

Amphotericin B, an antibiotic isolated from Streptomyces nodosus, is effective in the majority of cases.[5] Parker, et al,[6] report one failure among 43 patients treated. In their series, relapses occurred in 29% of patients receiving a total dose of less than 1.5 Gm. and in 4% of those receiving over this amount. A total dose of at least 2.0 Gm. commonly is recommended.[5] Relapses sometimes respond to a second course. It is agreed by most authors[5,12] that amphotericin B is probably the most effective drug. Most treatment programs are similar to that outlined by Parker, et al,[6] in which an infusion of aphotericin B dissolved in 1000 cc. of 5% dextrose in water is given starting with 5 mg. the first day increasing by 10 mg. daily until 50 mg. or 1 mg./kg. is attained. The time of infusion is from 3 to 8 hours. Fever, chills, and anorexia are associated with the infusion in a high percent of patients[14] and acute idiosyncrasy in the form of anaphylactic shock, thrombocytopenia, convulsions, and others sometimes occur. The injection of 25 mg. of hydrocortisone hemisuccinate into the I-V tubing appears to lessen the reactions associated with injection. Phlebitis is a problem which may be lessened by using scalp-vein or "butterfly" needles. Renal toxicity is the feature which limits the dose of amphotericin B which can be given.[15] Elevation of the BUN is found in over 90% and of creatinine in over 80% of patients treated. Occasionally this is associated with inability to conserve sodium. Hypokalemia is also reported. Tubular lesions associated with calcification have been reported in renal biopsies from patients receiving the drug. After treatment, the BUN and creatinine often remain somewhat above pre-treatment levels although within normal limits. Anemia apparently due to bone marrow suppression often occurs during treatment but red cell levels return to normal without treatment.[16]

Although considered to be somewhat less effective than amphotericin B,[12] 2-hydroxystilbamidine is effective and less toxic.[5,12] Lockwood, et al,[17] originally considering it the drug of choice now feel that it should be used only in the more slowly progressing cases. It is given in daily intravenous doses of 225 mg. until a total dose of 8 Gm. has been administered. Although stilbamidine was associated with severe neurotoxicity, reactions to 2-hydroxystilbamidine have been few; for example, in 23 cases Lockwood reports 1 case of rash, fever, and delirium, 2 of fever alone, and 1 of nausea and vomiting. Patients who fail to respond to one drug may respond to the other.

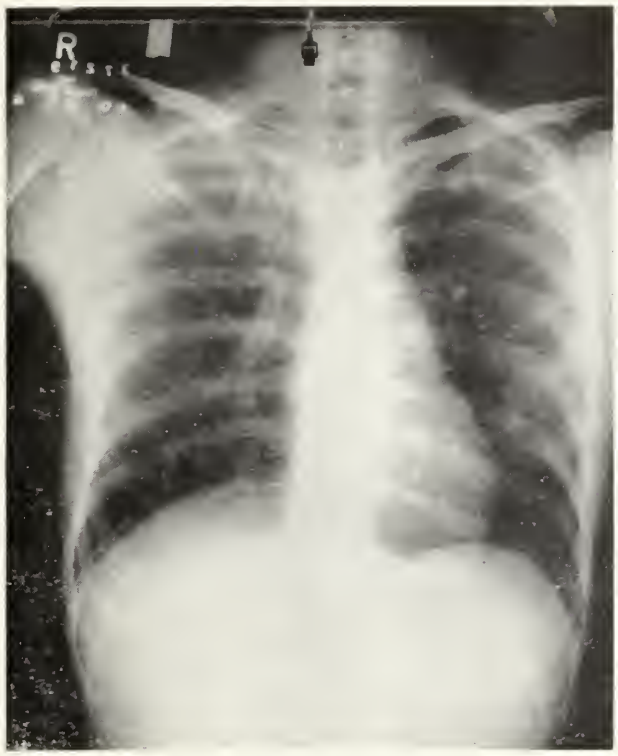

Fig. 1. P-A view of chest.

Fig. 2. A-P lordotic view of chest.

Whatever therapy is used, careful observation for relapses should be carried out for a period of several years.

Case Report

A 23-year-old, white male veteran who had lived all of his life in northern Aroostook County until 1966 when he was inducted into the army, spent his two years of military service at Fort Dix, N. J., in Louisiana, and in Viet Nam. A chest x-ray taken at the time of induction in 1966 in retrospect shows fine nodular and linear densities extending peripherally from the hila, especially marked in the left upper lung field but present bilaterally. In May of 1969, he developed fever with pain, redness and swelling of the left ankle and heel. Incision and drainage yielded pus from which Staphylococcus albus was grown. This was treated by antibiotics and a sequestrectomy of the left os calcis was performed in August. Amputation was advised and he was admitted to the VA hospital at Togus, Maine. He was thin, pale, and chronically ill and had a mild elevation of temperature. Examination of the chest, heart, lungs and abdomen were not remarkable. The left ankle was swollen with incisions below each malleolus draining a small amount of yellowish pus. There was a slight effusion of the left knee which was not tender. There were 6,446 leukocytes per cubic mm. of blood, 79% of which were neutrophiles, 21% lymphocytes; hemoglobin, 11.8 Gm./100 cc.; culture from the drainage from the left heel revealed Aerobacter group. The chest x-ray (Figs. 1 and 2) was interpreted as showing fine nodular markings bilaterally with poorly defined densities of the right apex and patchy densities without cavitation in the left first interspace. X-ray of the left ankle (Fig. 3) showed a completely destroyed left calcaneus with a few fragments of bone remaining. The left knee showed bone resorption in the femur and tibia adjacent to the knee joint and cystic areas in the lower end of the femur suggesting a destructive process.

On 9/11/69, because of complete destruction of the os calcis, a below-knee amputation of the left leg was performed and the pathological specimen showed granuloma. Upon review, this was found to contain giant cells and typical thick-walled yeast-like organisms of Blastomyces dermatitidis, some of which were budding (Fig. 4). At this time he was ill, febrile, and had a brief episode of left inguinal adenitis which subsided spontaneously. On 10/14/69, he developed a painful mass in the left upper arm which was incised and drained yielding a large amount of frank pus which was sterile on bacteriologic culture. First and second strength PPD tests were negative as was a blastomycin skin test. On 10/26/69, he was transferred to the Medical Service with a finding of anorexia, weight loss, and fever. Shallow, moist skin ulcers 1 to 2 cm. in diameter were observed on each forearm and he had a swollen tender right ankle from which pus was aspirated which contained the organisms of B. dermatitidis under direct microscopic examination.

Through the courtesy of Dr. Charles Okey, Director of the State Public Health Laboratory, serum was sent to the Fungus Serology Laboratory, National Communicable Disease Center, Leo Kaufman, Ph.D., Chief, for serological testing with the following results: Complement fixation test for blastomycosis 10/28/69, positive 1:16; 1/19/70, positive 1:8. Agar gel diffusion test with blastomycin positive on both occasions. Complement fixation tests for coccidioidin and histoplasmin were negative.

He was treated intravenously with amphotericin B beginning with 1.0 mg. in 1000 cc. of 5% dextrose and water which was buffered to pH 5.5 doubling the dose until a dose of 50 mg. was being given. Laboratory determinations of hemoglobin, white blood count, platelet count, serum potassium, magnesium, BUN, creatinine, SGO-T, and bilirubin were followed twice weekly. After the daily dose of 50 mg. had been reached, he showed a 2+ test for albumin in the urine, BUN rose to 31, and he had a chill after each dose. For this reason, the treatment schedule was changed to 50 mg. three times weekly and 25 mg. of hydrocortisone were added directly into the tubing of each infusion. On this schedule, the BUN remained

Fig. 3. X-ray of left ankle showing complete destruction of calcaneus and areas of osteoporosis in the tibia and talus.

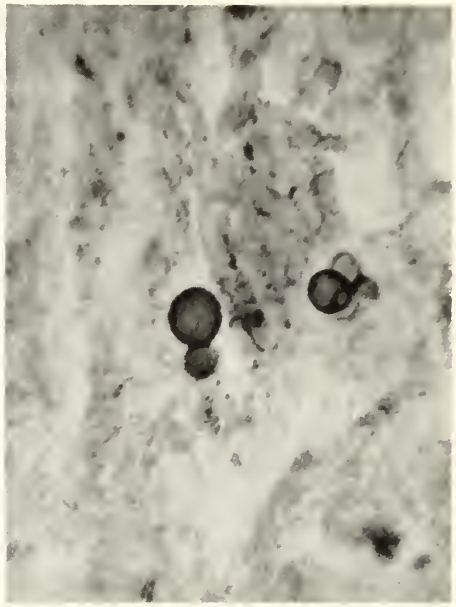

Fig. 4. Photomicrograph showing B. dermatitidis organisms in section from amputated foot. Silver methenamine stain X 970.

between 20 and 31; urinary albumin varied between negative and 1+ with occasional showers of hyaline and granular casts. Except for a two-week intermission over the Christmas holiday, treatment was continued until a total dose of 2.5 Gm. was reached. The treatment extended from 10/26/69 to 3/5/70. Evidence of mild hemolytic anemia was detected during December when a hemoglobin of 9.0 Gm. and a reticulocyte count of 12.2% were found. There was an episode of leukopenia in January from which the patient recovered spontaneously without omission of the drug. The lowest white blood count was 2,754 on Jan. 16, 1970, with 78% neutrophiles. No reduction in platelet count was detected. During the periods of anemia and leukopenia, bone marrow aspirations revealed normal cellular patterns. During treatment, the skin lesions healed, the effusion in the left knee joint disappeared, and a weight gain of 15 pounds occurred. Sedimentation rate (Westergren method) receded from 110 mm./hr. at the time of admission to 34 mm./hr.

He was discharged from the hospital with a well-fitting prosthesis on March 6, 1970, and will be followed at intervals of one to two months for the next several years. A chest x-ray at the time of discharge was essentially unchanged from the admission film.

Summary

The second reported case of systemic North American blastomycosis apparently originating in the State of Maine has been described. This serious systemic fungus infection thought to be acquired through the inhalation route is seen primarily in Central, Southern, and Southeastern United States. Personal communication with other physicians[2] has revealed that apparently there have been a total of four proven cases of North American blastomycosis known to the medical profession in Maine, at least three of which may have been acquired in northern Aroostook County, suggesting that there may be a focus of this organism in that area.

This disease has been reported to involve numerous organ systems of the body, the skin and lungs most commonly. An unusual manifestation in this patient was involvement of the ankle joint with the apparent occurrence in the knee joint. Other tissues involved in this patient are lungs, subcutaneous tissue, skin, and bone. Prior to 1951, when the stilbamidines were introduced as treatment for B. dermatitidis infections, the prognosis was extremely poor with a reported mortality rate of 80%. Presently, amphotericin B and 2-hydroxystilbamidine are effective drugs and result in cure in a majority of the cases. Relapses may occur and long-term follow-up is required. The disease should be suspected in any illness having otherwise unexplained pulmonary, osseous, and constitutional manifestations. Diagnosis depends on culture of sputum including material from gastric washings, pus, or material obtained from biopsy or joint aspiration. It is emphasized that currently available skin test material apparently is unreliable diagnostically.

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Continued on Page 150

Lithium Carbonate

A Dangerous but Useful Drug

JAMES C. WREN, M.D.*

April of 1970 marked a milestone in medical history as the Food and Drug Administration announced the release of lithium carbonate for use in psychiatry. For the first time, a specific drug treatment for a specific psychiatric illness – the manic phase of manic-depressive disorders – became available. In addition, the relatively simple measurement of lithium in the patient's serum as an objective guide to treatment is another "first" in psychiatry. By contrast, standard treatment for mania such as electroshock and chlorpromazine has to be considered symptomatic treatment and objective measurements to guide their dosage are impossible or impractical. However, the use of lithium requires that accurate psychiatric diagnosis, meticulous medical evaluation, and complete laboratory facilities be available.

Examination of the history of lithium reveals evidence of both toxicity and efficacy. It was used in medicine over one hundred years ago but there is little evidence of its significant use before 1949. Cade[1] in Australia introduced lithium salts into psychiatry in 1949 when he successfully treated manic excitement with lithium carbonate. During the next ten years, many studies were conducted in Australia and Europe. Schou[2] in Denmark was the most active investigator publishing numerous papers confirming the efficacy of lithium in manic states. Meanwhile in the United States in 1949 the unrestricted use of lithium chloride as a salt substitute for cardiac patients resulted in much toxicity and four deaths. This disaster caused by insufficient knowledge of the mechanism of lithium's action resulted in widespread lack of enthusiasm for the drug. The development of other drugs along with the demonstration of the narrow range between the therapeutic and toxic dose of lithium further delayed any extensive studies. It was not until the early 1960's that scattered studies of lithium in psychiatry began in this country. Since 1965, the major clinical work has been conducted in the United States and Scandinavia. Some idea of the extent of recent studies is obtained by examining a recent publication by the Veterans Administration Central Neuropsychiatric Research Laboratory of a bibliography on the clinical use of lithium in which five hundred and ninety-two references are listed.

The present general clinical usage of lithium carbonate is limited by the Food and Drug Administration to manic disorders in which the success rate has been extraordinarily high. Other usage continues to be the subject of much investigation. The investigative prophylactic use in both mania and chronic depression promises exciting development in the future. Still other investigations have already suggested that lithium is not effective in schizophrenia, acute depression, and organic brain syndromes.

Lithium carbonate has been produced as a capsule or tablet containing 300 mg. each. The initial daily dose in acute mania is usually 600 mg. rapidly increasing within two to three days to 1200 to 1800 mg. in divided doses. Some severe cases may require 2400 mg. daily for a short period gradually reducing to a maintenance dose of 600 to 1200 mg. as symptoms are controlled. It should be noted that the use of lithium and electroshock or chlorpromazine concurrently is permissible if the clinical situation warrants it. The main disadvantage of lithium is its slower action – maximum effect may require five to ten days.

The monitoring of treatment by frequent serum lithium determinations is essential. Appropriate special equipment for these measurements is an absolute prerequisite to its use. The generally accepted therapeutic levels of lithium in the serum ranges from 0.5 mEq./L. to 1.2 mEq./L. Toxicity may occur at levels of 1.5 mEq./L. In severe cases, levels up to 2.0 mEq./L. for short times may be necessary for control of symptoms. Absorption studies have indicated that blood should be drawn for lithium determinations not less than eight nor more than twelve hours after the last dose. In the acute treatment phase, serum lithium levels should be done at intervals of one to three days. Weekly checks should be done for one to two months establishing maintenance dose. In the longer term investigative prophylactic studies, monthly monitoring has been found to be usually satisfactory.

Despite extensive study, the mechanism of lithium's action remains unknown. The two major bodies of data are concerned with catecholamine metabolism and electrolyte metabolism. With its unique measurability, lithium has opened up many areas of psychiatric research. Its influence on mania is established while its beneficial prophylactic effect on the apparently opposite state, chronic depression, seems promising. This suggests then some common denominator for these pathological mood states.

It has been suggested that norepinephrine in the central nervous system is increased during mania and reduced during depression and that lithium decreases norepinephrine available to adrenergic receptor sites. This theory might explain its effectiveness in mania but is an

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unsatisfactory explanation for any efficacy in depression. As for electrolytes, there is a close relationship between lithium and sodium. An increase in residual sodium has been found in both mania and depression. Administration of lithium has been shown to bring about marked changes in electrolyte distribution in animals. Kline,[4] a strong advocate of the prophylactic use of lithium, has suggested that gradual alteration of the relationship between sodium and potassium in time may account for the crucial clinical fact that the longer lithium is given the shorter and milder are the attacks of affective disorders. Magnesium has been found elevated consistently after lithium treatment. Since magnesium is said to be critical to the transport of sodium and potassium to nerve, it may be that alteration of magnesium by lithium may be an important aspect of the lithium effect.

Lithium toxicity may occur as a result of an excessive dose or from accumulation due to undetected renal insufficiency. Once a patient's maintenance dose is established the kidneys must excrete as much lithium as is administered in order to prevent excessive serum levels. Other obvious causes of excessive serum levels are overdosage and failure to obtain blood samples at proper intervals after the drug is taken. In any case, if a serum level is reported above 1.5 mEq./L. the drug must be stopped and the reason for it determined before re-starting at a lower dose.

A long list of precautions, warnings, and adverse reactions have been detailed adequately in the manufacturer's package insert and in Current Drug Information sent to all physicians by the Food and Drug Administration. All who plan to use lithium should be thoroughly familiar with this material and with the fact that full-blown lithium intoxication is a catastrophe requiring intensive care similar to that required for severe acute barbiturate poisoning.

Long-term effects of lithium on the thyroid have received much attention. In fact, the importance of these effects has been over-emphasized in some reports. There is evidence that lowering of the protein-bound iodine and elevation of the ^{131}I uptake may occur during the lithium therapy. Goiter formation apparently related to lithium has occurred. Schou, *et al*[5] and Cooper and Simpson[6] have found the incidence of goiter formation exceedingly low. All of these effects are reversible by stopping the drug or by the administration of thyroid.

Summary

In summary, a listing of indications and contraindications for the use of lithium, both psychiatric and medical, seems appropriate along with laboratory requirements:

1. Psychiatric:

A. Indications – the manic phase of manic-depressive disorders.

B. Contraindications – (1) Schizophrenia, acute depression and (2) Organic brain damage.

2. Medical:

A. Indications – None.

B. Contraindications – (1) Any significant cardiovascular disease. Patients with symptomatic atherosclerosis should be probably avoided and congestive heart failure is an absolute contraindication; (2) Renal disease. Any condition associated with any degree of renal failure is an absolute contraindication; (3) Any condition requiring low sodium intake; (4) Any condition requiring diuretics; and (5) Any organic disease of the central nervous system.

3. Laboratory: Standard complete laboratory facilities must be available including adequate thyroid function tests, along with equipment for the immediate determination of serum lithium. Measurement is most accurate with an atomic absorption spectrophotometer although less precise but clinically adequate levels may be obtained with certain types of flame photometers.

It is evident that the use of lithium carbonate in psychiatry requires a team effort. Inadequate psychiatric diagnosis, medical evaluation, or laboratory support could give poor results or even result in disaster.

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Prevention of Sudden Death from Coronary Disease Through Pre-Coronary Care

JACOB B. DANA, M.D.*

On Oct. 16, 1793, John Hunter, who had had angina pectoris for 20 years, died suddenly of what was determined at autopsy to be severe coronary artery disease. Sudden death and its association with coronary disease had been described as early as the 16th century by Leonardo da Vinci.

In the last seven years, attention has been focused on the treatment of patients with acute myocardial infarction who survive long enough to reach a medical facility. The development and success of coronary care units has demonstrated that most life-threatening arrhythmias can be treated effectively if recognized early. However, we realize now that two-thirds of the patients who experience acute myocardial infarction die before they reach the hospital. Since there are approximately 600,000 deaths yearly from acute coronary disease and since 400,000 of these occur outside the hospital, we are obliged to re-examine the problem of sudden death.

Sudden death during an acute heart attack is probably the greatest therapeutic challenge of the moment. Our success in the CCU in the prevention and treatment of cardiac arrest serves to emphasize our failures outside the hospital.

An appraisal of the impact of sudden and early death in acute myocardial infarction and of ways in which it might be predicted or prevented is sorely needed.

From 40 to 75% of the deaths from acute myocardial infarction take place during the first hour, and there is a high risk throughout the rest of the first 24 hours. By the end of 24 hours, 30 to 40% of all patients with acute myocardial infarction have died and this accounts for 60 to 90% of all deaths. Essentially, mortality is an exponential function of time. As each hour passes, the risk of death decreases.

Kuller in a study of sudden death in Baltimore showed that 60% of patients under 65 died either at home or in transit before treatment could be given. From this Public Health Service survey came the strong suggestion that although these deaths were sudden, they were not without warning. Twenty-three percent of these patients had seen a physician in the previous week. This point is emphasized by another report that of 100 patients reaching a CCU, 65 had symptoms preceding the acute symptoms in the previous month.

While it may be difficult, though not impossible, to expect to achieve a substantial lessening of the number of patients dying within one hour of onset of acute symptoms, more attention should be devoted to the possibility of the application of coronary care at an earlier stage for those who may die later in the course of their acute illness.

The longest delay results from the time it takes the patient to call the physician and the next delay results from problems in obtaining the services of a physician. There is a delay then in transporting the patients at risk and the frequent delays on the admitting or emergency floors which many times may be due to lack of proper diagnosis.

The patient's interpretation of and reaction to his symptoms sometimes causes a crucial time delay in the decision-making process before medical care is sought. The interplay among symptoms, patient rationalization of the impact of symptoms, and his ability to obtain medical advice occupies an average of 6 to 8 hours of therapeutically important time since it is presumed that many sudden deaths due to myocardial infarction occur during this time period. It is known that ventricular fibrillation is 25 times as common in the first 4 hours after onset than it is subsequent to that time.

How do we identify those patients who are particularly liable to die suddenly or early in the course? Some facts are known:

A substantial proportion of those dying early have had a previous myocardial infarction or angina pectoris. More have had symptoms of ischemic heart disease that have gone unrecognized or been misinterpreted. As mentioned earlier, almost a quarter of those dying suddenly have consulted a physician in the preceding week. Patients with A-V or intraventricular block and patients with PVCs appear to have a greater risk of sudden death. In addition, there is a substantial risk in patients with recent onset of angina or exacerbation of pre-existing angina. The risk is greater with a sudden recurrence of angina than with an exacerbation of pre-existing angina.

The Framingham study suggests more sudden death in obese patients and particularly those with elevated cholesterol, diastolic blood pressure elevation, or diabetes. Heavy cigarette smoking is also a factor present in the many who die suddenly.

Two areas require careful study: One is the relation of sudden death to preceding health and the study of other possible risk factors about which there is little information at present. A second major problem is the mechanism through which the acute heart attack leads to sudden early death.

The hypothesis is that sudden ischemic death of the ambulatory patient is the result of electrical instability.

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This is clinically demonstrable by ventricular premature beats (VPB) and by bradycardia, either or both of which may result in ventricular fibrillation.

The strategics intended to identify and protect the potential victim are designated as pre-coronary care.

A sound program of pre-coronary care requires simultaneous ongoing investigation as well as reorganization or reorientation of treatment programs. The objective is to test the hypotheses and begin the application of the lessons learned in the operation of CCUs.

Investigation must be oriented to the problem of how to single out the potential victim from within the larger community of coronary patients. The crucial question is whether electrical instability presages the occurrence of sudden death. If electrical instability is mainly or only associated with the terminal event, then extensive monitoring of a large population is unnecessary and wasteful. What is needed is to monitor the *high risk* coronary population and to relate the incidence and type of ectopic activity prospectively to clinical outcome. Passive monitoring may not adequately identify electrical instability and provocative measures such as carotid sinus stimulation or mild exercise may be needed to unmask such instability. (Dr. Lown – 5 min. exercise = 2 hours monitoring)

There are two points which offer great promise for shortening the pre-hospital phase of coronary care. First is a sharper definition of prodromal and early symptoms which could be available to the population at risk and to physicians. This should reduce the current delay in entry of the patient into the coronary care system. Secondly, the coronary care system can be improved to minimize the delay in applying effective treatment particularly in control of arrhythmias.

Reduction of the toll of sudden coronary death need not await the results of future investigations. A pre-coronary care activity that can be utilized widely now involves the stabilizing of heart rhythm at the very inception of a major coronary episode. This involves the use of atropine, lidocaine, or a combination when appropriate. Use of these agents by paramedical personnel would obviate the need for costly, elaborately equipped, mobile CC ambulances. There should be pre-coronary care areas in community health centers and hospitals to obviate present delays. The organization of pre-coronary care areas for monitoring, screening, and triage during the earliest stages is worth considering.

A further pre-coronary care strategy is the initiation of anti-arrhythmic drug prophylaxis programs for high-risk patients. The interval between onset of the acute episode and catastrophe is too short for effective medical care. Anticipatory measures may well be indicated. Pilot studies with suitable anti-arrhythmic drugs are essential to define guidelines in their usage and to determine the nature and incidence of adverse reactions.

Sudden death in the community is a major problem in cardiology. Unlike other catastrophes it is reversible. Death most probably results from ventricular fibrillation due to an ischemia-induced state of electrical instability. Again, these events are preventable in a CCU. Recognition of the susceptible subject and development of measures aimed at preventing sudden death constitute the domain of pre-coronary care. The VPB appears to be a shibboleth for clinically identifying the patient at risk.

To re-emphasize, proper utilization of a pre-coronary care area would require lay and physician education on the nature of symptoms, reasons for need of prompt monitoring with the onset of symptoms as well as the importance of preventive measures in promoting coronary health.

A critical problem is to design the operation of pre-coronary care so that in each community it makes the most effective use of personnel and resources available. Evaluation of the effectiveness of each program must be an integral part of the initial planning. If a program is effective, there should be a decline in both the death rate from ASHD and total death rate in the community.

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Some Roles of a Psychiatric Hospital

CHARLES ROTHSTEIN, PH.D.*

The vast majority of patients voluntarily or involuntarily admitted to a psychiatric hospital are telling us in eloquent terms that they are unable to cope with the stresses of their environment. This message is, or should be, crystal clear to us regardless of the symptom language in which this message is cloaked. The schizophrenic, the paranoid, the alcoholic, the passive-aggressive, the passive-dependent, the depressed, the anxious, the somatizer, the acter-outer, are all telling us that life outside of the hospital is beyond their ability to handle, regardless of whether this inability denotes that a major stress has overwhelmed a basically adequate character structure or a minor stress has capsized a basically inadequate character structure. And, while it is hardly fair to expect that patients will spontaneously recognize this state of affairs it is not unfair to expect that psychiatric hospital staffs should recognize it and make their plans accordingly.

Once a patient has been admitted to a psychiatric hospital, presumably as testimony to his failure to cope with the stresses of life, the hospital can play various roles with him. The role that it chooses to play should depend upon its analysis of two cogent variables – the nature of the patient's basic character structure and the nature of the environmental stresses that led to his hospitalization. By basic character structure, we refer to those characteristic attitudes, cognitions, and instrumental skills with which a person confronts life and attempts to meet his needs. By environmental stresses, we refer to those changes in the patient's environment that render him incapable of satisfying his needs with his existing character structure.

The first question that a hospital should ask at the time of a new admission is: How adequate is the basic character structure of the individual? Assuming a bipolar dimension of character structure anchored on one end by the term "adequate" and at the other end by the term "inadequate" the person should be assessed relative to his position along this dimension. A character structure toward the adequate pole of this dimension would be exemplified by an individual who historically has shown himself capable of meeting personal and social needs in a wide range of environments. A character structure toward the inadequate end of this dimension would be exemplified by an individual who historically has shown himself incapable of meeting personal and social needs save in the most benign or restricted environments. For example, a patient who has historically demonstrated a relatively consistent ability to relate to peers and authorities in a rational and constructive fashion and who has been able to structure and pursue realistic achievement goals compatible with the expectations of his significant figures and his culture would be rated on the adequate end of the dimension. Conversely, a patient who has shown historically a relatively consistent inability to relate to peers and authorities in a rational and constructive fashion and/or an inability to structure and pursue realistic achievement goals compatible with the expectations of his significant figures and his culture would be rated on the inadequate end of the dimension. The number of rating points along this bi-polar dimension would be limited only by the ability of the assessors to make judgments utilizing the criteria noted above. Consistent with this approach, if a patient is scored on the adequate end of the character structure dimension, we must assume that he has been overwhelmed by a major environmental stress. Conversely, if a patient has been rated at the inadequate end of this dimension, we must assume that the environmental stress which overwhelmed him is probably minor in nature. In essence, the environmental stress in the former case can be conceived of as a major environmental wave while in the latter case it is probably more in the nature of an environmental ripple. Subsequent to an assessment of the relative adequacy of the basic character structure of a newly admitted patient, the hospital can play various roles in the treatment process. Essentially, we will consider three major roles that the hospital can play subsequent to such an assessment.

First, if the hospital determines that an individual has a basically adequate character structure that has been overwhelmed by a major environmental stress – for example, unexpected loss of one or more key significant figures, unexpected loss of achievement potentials or positions, major social upheavals – it can do one or combinations of the following: (a) it can serve as a temporary holding and supportive unit for the patient while the major environmental stresses spontaneously pass at which time it returns the patient to his pre-hospital environment; (b) it can serve as a temporary holding and supportive unit while the hospital staff intervenes in the patient's pre-hospital environment to attenuate the major stressors – for example, family therapy, vocational advice, or placement – after which it can return the patient to his pre-hospital environment; (c) it can serve as a temporary holding and supportive unit while pointing out to the patient those environmental stresses that overwhelmed him and encourage him to take action to produce the necessary changes in his environment – for example, searching for new significant figures, vocation or job change, moving to a less destructive environment. Essentially, in this role the hospital serves as a temporary escape and support agent until the environmental stress

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has passed, been changed by the hospital, or changed by the patient. In this role, the hospital does not attempt to meaningfully change the basic character structure of the individual but rather serves as a holding unit for a period of time until the necessary environmental alterations – spontaneous, hospital, or patient-generated – have taken place.

The second major role that a hospital can play involves the treatment of those patients who have been judged to have a basic character structure intermediate on the adequacy-inadequacy dimension. For these patients, the hospital can attempt to play the role of motivator and teacher. Through the utilization of appropriate motivational and teaching techniques, it can attempt to change the character structure of the individual to make him more capable of dealing with a wide range of extra-hospital environments. This can be accomplished through various rehabilitation techniques such as insight therapies, milieu therapy, behavior therapy (operant and classical), and token economies. In this approach, the hospital utilizes its resources to make the maximum change in an individual's character structure that it realistically can and then considers those extra-hospital environments in which the modified character structure has a good potential to function successfully. Assuming unqualified success in character structure modification, the patient can be placed in almost any extra-hospital environment. Assuming more modest successes in character restructuring, the patient may be placed in more restricted extra-hospital environments; for example, a day/night hospital, quasi-protected family settings, foster home placement, continued outpatient treatment. This second role of the hospital emphasizes heavily character structure alteration to whatever extent possible, with subsequent extra-hospital placement paralleling the relative adequacy of the modified character structure. Here the hospital plays the role of both patient change agent and environmental router in whatever proportions indicated by the individual case. In any event, this role should be of a time-limited nature accepting the fact that once a patient has reached a plateau in the character change process immediate plans should be made for his extra-hospital placement as continued hospitalization beyond this plateau point will only make eventual placement more difficult.

The third role of the hospital is played when a patient is encountered with such a basically inadequate character structure as evidenced by past repeated failures to adapt to even the most protected environments that the probability of meaningful character change is almost nil, given our present resources. When such a patient is encountered, it is often tempting for the hospital to try character change. However, the lessons of history suggest to us that this would probably result in a net waste of available resources better utilized with other populations. At best, we might try a brief crash program of techniques to assess the probability of inducing meaningful character change. However, failure of these techniques after a brief but energetic trial should orient us to accepting the necessity of finding benign extra-hospital placements for this type of patient; for example, sheltered workshops, nursing homes, foster homes, protected placement with relatives, domiciliary facilities. Here, too, it is essential that the hospital treatment be time-limited or else the hospital will soon find itself glutted with this type of treatment-refractive patient who attempts to make the hospital his permanent home, such a glut reducing drastically our capacity to have a meaningful impact upon more treatment-amenable patients.

In brief, we are suggesting that at the time of admission to a psychiatric hospital each patient be assessed relative to the adequacy of his basic character structure and the nature of the environmental stress that precipitated the hospitalization with a time-limited treatment program planned subsequent to such an analysis. To a large extent, our analyses should consider historical facts relative to previous ability to effectively deal with environments which the patient has encountered. The failure to conceptualize patients and treatment along this or a similar dimension results in a pitiful waste of our resources. We have at our disposal the techniques, albeit not in a perfect stage of development, to make such an assessment of patients and to formulate rational treatment plans at the time of admission. The attempt to structure generic or specific treatment programs without such an assessment makes of the rehabilitation process a chancy, random, and inefficient affair which does a disservice to patients, staff, and that society which pays us to be the experts in this area.

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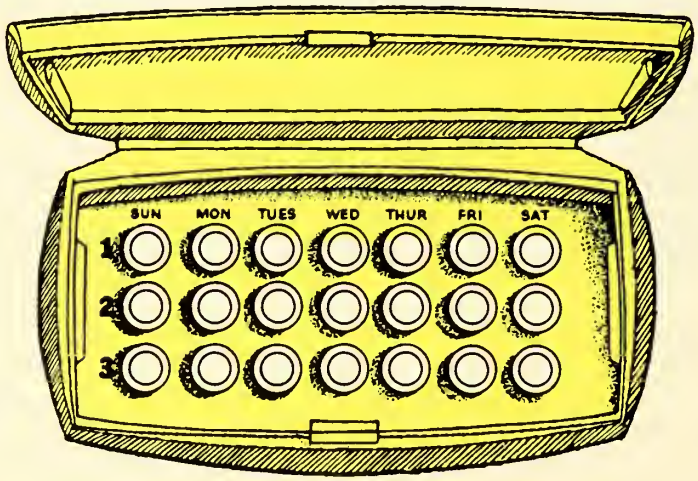

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Special note: Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Demulen is indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration, and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear, since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Demulen. Therefore, if such tests are abnormal in a patient taking Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Demulen may mask the onset of the climacteric. The pathologist should be advised of Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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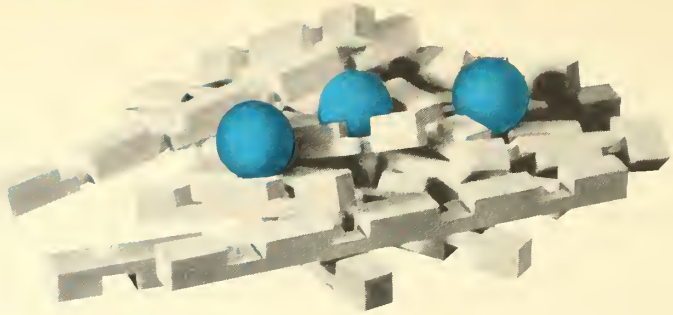

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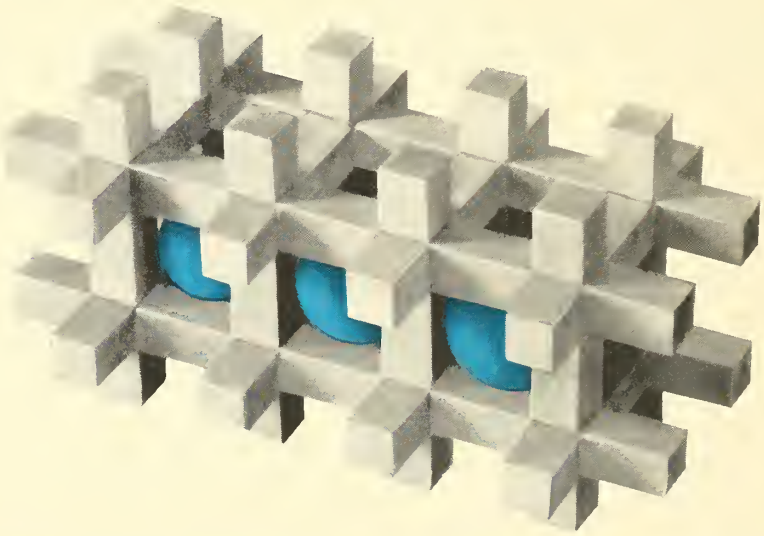

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Contraindications: Glaucoma, urinary bladder neck or pyloric obstruction, duodenal obstruction and cardiospasm. Hypersensitivity to any of the ingredients.

Warnings: Do not exceed recommended dosages.

Precautions: Administer with caution to persons with known idiosyncrasy to atropine and cardiac disease. While under this therapy the urine is blue; patients should be so advised to allay apprehension.

Adverse Reactions: Neither irritation nor untoward reactions have been reported; however, if pronounced dryness of the mouth, flushing, or difficulty in initiating micturition occurs, decrease dosage. If rapid pulse, dizziness or blurring of vision occurs, discontinue use immediately. Acute urinary retention may be precipitated in prostatic hypertrophy.

Dosage and Administration: Adults: Two tablets, orally, four times per day, followed by liberal fluid intake. Older children reduce dosage in proportion to age and weight.

How Supplied: Bottles of 100, 500 and 1,000 tablets.

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Duodenal Stump Closure Using Ox Fascia

SIDNEY H. SOBEL, M.D.,* STANLEY E. SCHWARTZ, M.D., F.A.C.S.** and PHILIP COOPER, M.D., F.A.C.S.†

Since the early twentieth century, investigators in tissue transplantation have studied fascia lata as autogenous, homogenous, and heterogenous graft material. In 1917, Neuhof[1] transplanted autogenous fascia lata to defects in the wall of the urinary bladder, the stomach, the esophagus, and the trachea in dogs and reported several experiences using autogenous fascia lata in humans. He referred to a report published in 1909 by Kirschner regarding a successful autogenous graft of fascia lata in dogs involving the simple transfer of the tissue from one tissue bed to another.

Koontz[2] in 1929 successfully repaired visceral defects in dogs using an iodized-alcohol-preserved preparation of ox fascia lata. Koontz[3] reported on the use of this preparation in closing abdominal wall defects in humans. This material has been employed with success in closing defects in the human chest wall[4,5] where its suture holding quality, pliability, tensile strength, and resistance to infection make it especially desirable. Our own experience using this tissue for similar purposes has been encouraging.

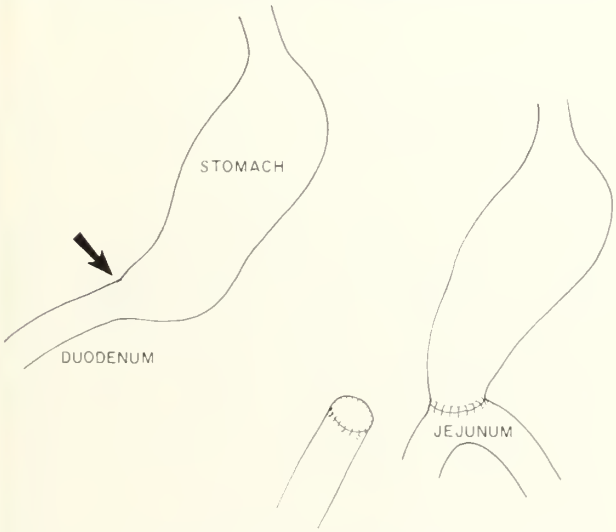

Fig. 1. (a) Normal stomach and duodenum of the dog in diagrammatic form. (b) A completed Billroth II partial gastrectomy; the duodenum has been closed with an ox fascia lata graft.

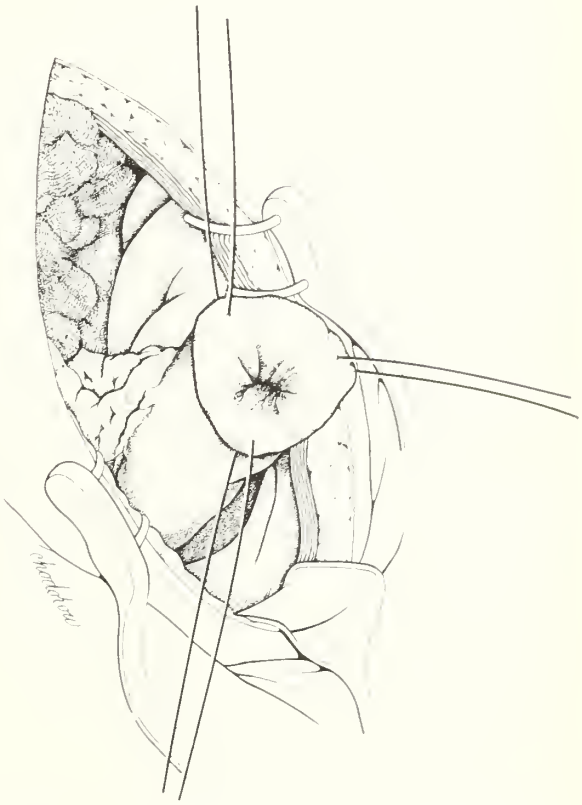

Fig. 2. Duodenum with three stay sutures holding the stump open.

Although alcohol-preserved-ox fascia is tolerated remarkably well by both canine and human hosts, its ultimate fate in the host is not yet established with certainty.[6]

MATERIALS AND METHODS

An experiment was designed to test ox fascia lata as a cap closure for the duodenal stump in dogs, having in mind the ultimate application of such a graft in the management of some difficult duodenal stump closures in humans.

An iodized-alcohol-preserved preparation of ox fascia lata was obtained from a South American laboratory‡ for use in the study.

Eight mongrel dogs weighing 20 to 50 lbs. were used without regard to sex, age, or breed characteristics. No

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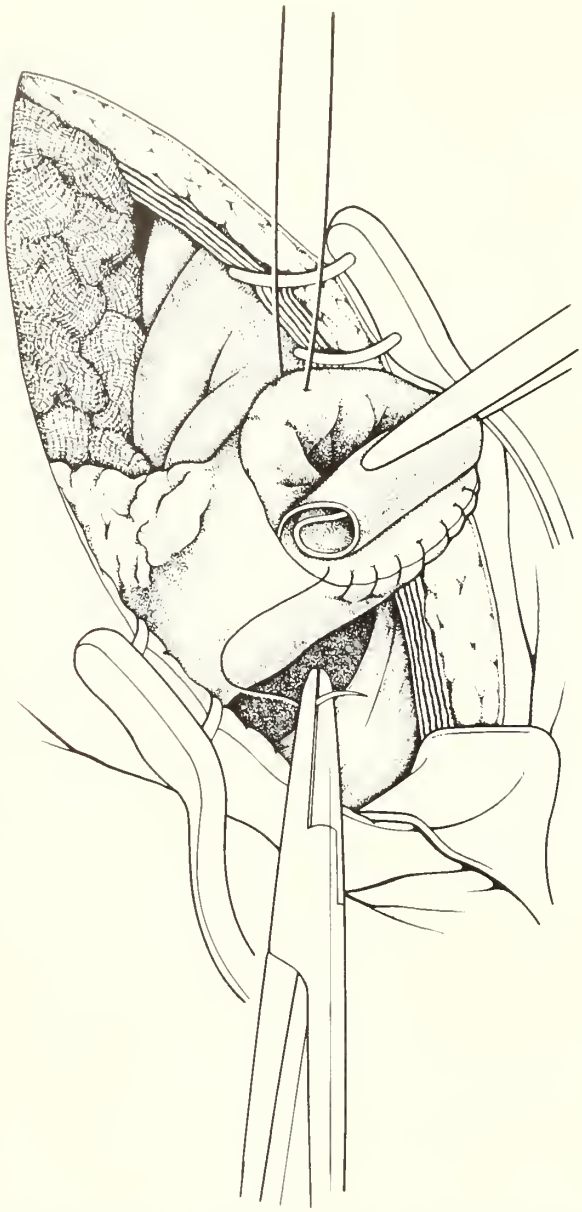

Fig. 3. Partially closed duodenal stump showing edge-to-edge approximation of ox fascia and duodenum by placement of a continuous suture.

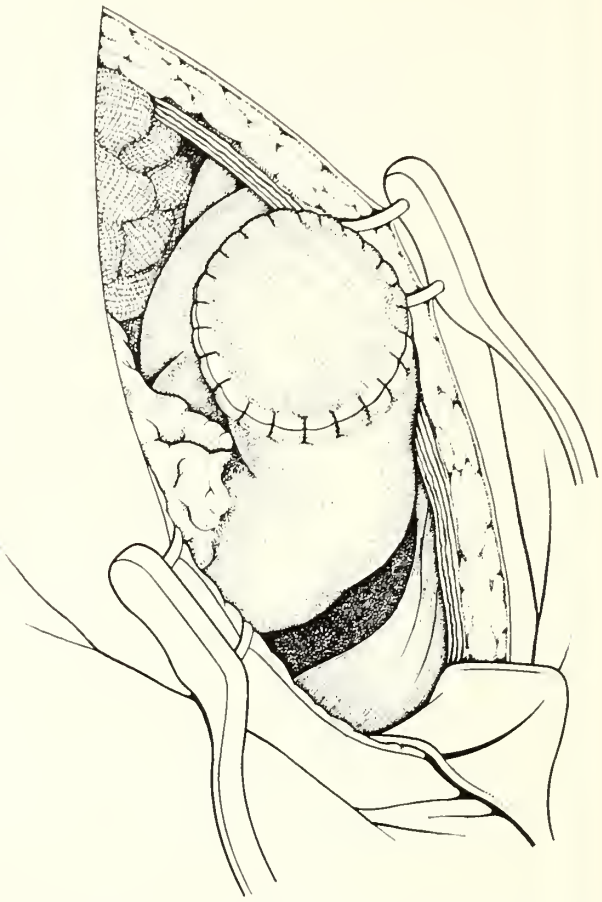

Fig. 4. The completed closure of a duodenal stump with an ox fascia lata graft.

other experimental procedures had been performed on these animals.

The animals were fed only water for the twelve hours prior to surgery. Under intravenous pentobarbital anesthesia a Billroth II type of partial gastrectomy was performed (Fig. 1). The duodenal stump was closed with a patch of ox fascia lata cut to the shape of and a size slightly larger than the duodenal stump opening. Three stay sutures of silk were placed equidistant through the seromuscular layers to hold the duodenal stump open (Fig. 2). The ox fascia lata patch was then sutured to the stump opening with a continuous 3-0 atraumatic silk suture, which first traversed all layers of the duodenal wall from serosa through mucosa, and then through the fascia lata from the inner surface outward. Bites of the continuous suture were placed approximately 4 mm. from the cut margins of both duodenum and fascia and approximately 6 mm. apart (Fig. 3). By so placing the sutures, the graft did not overlap the cut margin of the duodenal defect. Rather, the transplant was sutured into the defect so that an edge-to-edge approximation was obtained between fascia and duodenum. At the completion of this closure a liquid-tight seal was always apparent (Fig. 4). According to Neuhof,[1] this method of suture greatly enhanced the ease of organization and healing of the graft to the host tissue and was essential for prevention of leakage.

Postoperatively, the dogs were fed only water for twelve hours and then were advanced from a diet of rice meal and milk to a standard diet of horse meat and "kibbled" dog meal. Terramycin® and Berocca®-C were given intramuscularly for the first five postoperative days.

Animals were reoperated at 2 weeks and 2, 6, and 18 months postoperatively, two animals at each interval, and the duodenal stumps were inspected and amputated for pathological study. The amputated stumps were

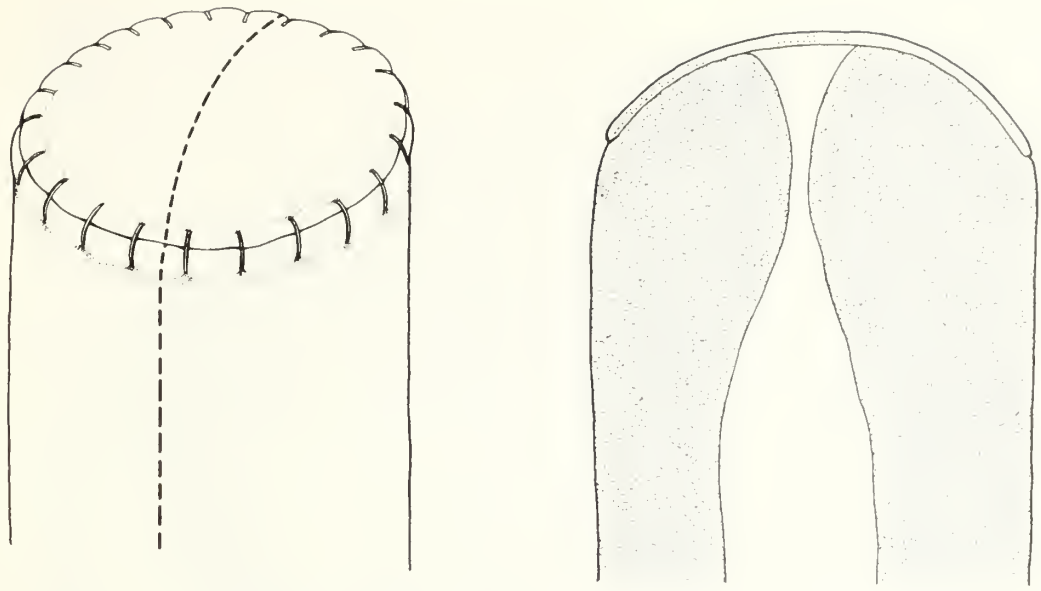

Fig. 5. Technique of sectioning duodenal stump for histopathological study.

opened across their diameter as shown in Fig. 5 and sections prepared and stained with hematoxylin and eosin, Masson trichrome for connective tissue, and in some instances Gomori and Verhoeff stains for elastica.

Results

At the conclusion of the study in all the dogs, the duodenal stumps were healed. The diameter of the suture line between fascia and duodenum had not narrowed significantly suggesting that there was little drawing together of the edges of the duodenal stump during the operation and the healing process.

At two weeks postoperatively, the histological sections of the duodenal stump showed some ingrowth of fibroblasts under and into the fascia lata (Fig. 6).

At two months postoperatively, the fascia lata was seen as a hyaline layer with fibroblasts outside the fascia lata. The inner surface of the fascia lata was lined by mucosal epithelium.

At six months and eighteen months postoperatively, there was some elastification of the fascial layer and an ingrowth of small blood vessels and fibroblasts into the fascia and the mucosal epithelium covering the inner surface of the fascia but muscle layers were absent from this area (Fig. 7).

At eighteen months postoperatively, the histological findings were essentially the same as those noted in the six months specimen.

Fig. 6. Section of duodenal stump two weeks postoperatively.

Discussion

Though Neuhof[1,7] recognized fascia lata as the most promising of the graft materials available to repair defects in the wall of the esophagus and the trachea, he reported a singular lack of success in the application of autogenous fascia lata grafts to defects in the upper small intestine. As the grafts were applied lower in the intestinal tract, the results were better although never reliable. He stressed the importance of a water-tight seal in closing defects in the gastrointestinal tract with a fascial graft. In a preliminary experiment, we noted that a loosely applied fascial cap led to the early demise

Fig. 7. Section of duodenal stump six months postoperatively.

of the animal from leakage of intestinal fluids through the suture line.

Koontz[8] postulated that the alcohol preservation technique used with the fascia lata may lessen the foreign protein reaction by destroying antigen. We bring this up to stress again our observation of the remarkable acceptance of this graft material by the host.

Throughout our experiments, the fascial layer was apparent at the site of the original ox fascia lata graft. Some workers believe that the foreign graft is gradually replaced by host tissues.[3] Chandy[9] examined specimens of ox fascia buried for four years in human tissue. Although he was able to identify the ox fascia grossly as a distinct fascial layer, he demonstrated an ingrowth of host blood vessels and exudate both within and outside the graft which led him to believe that the foreign graft was gradually being replaced by host tissue. Peer[6] has expressed a similar opinion based on his observation of grafts examined up to eight months after transplant.

It is interesting to note that mucosal epithelium in the duodenum as in the mouth migrates to cover or line a raw fascial surface at an early stage of healing.

Summary

In a group of eight dogs subjected to partial gastrectomy, the duodenal stump was closed with a round patch of iodized-alcohol-preserved ox fascia lata cut to a size slightly larger than the diameter of the duodenal stump and sutured in place with a continuous fine silk suture so as to produce a water-tight seal. Amputation biopsies of the duodenal stumps were performed at intervals ranging from several weeks to one and one-half years. This heterogenous fascial graft was accepted remarkably well by the foreign host. It was bridged on its inner surface by mucosa alone; the muscular layers never crossed the fascial graft site. Though a fascial layer persisted across the stump throughout the length of the experiment, it cannot, under the conditions of this experiment, be concluded whether the fascial layer at the stump represents the original ox fascia, vascularized and elasticized and vitalized by the host, or host tissue that gradually replaced the ox fascia as the latter was resorbed.

In these animals the duodenal stumps were safely, easily, and effectively closed. Such a graft might greatly simplify the handling of certain difficult duodenal closures in human gastric surgery.

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Blind Rehabilitation Program Physical Medicine and Rehabilitation Service Veterans Administration Center, Togus, Maine

James J. Mahaney, B.S., C.C.T.

The Blind Rehabilitation Program at Togus was started in 1964 by the former Chief of Physical Medicine and Rehabilitation, Dr. Emma Varnerin. It was integrated as a part of the Corrective Therapy Program.

Under the Chief, PMRS, James J. Mahaney, Certified Corrective Therapist, is responsible for this phase of rehabilitation. Mr. Mahaney received training in "Blind Rehabilitation, Orientation and Mobility Training" at the VA Hospital, Hines, Illinois.

Patients are assigned to the Blind Rehabilitation Program by referral by the case physician. The patients are first examined by the Ophthalmologist who gives the pathology and recommendations concerning the patient's eye condition. This procedure is very important, particularly if the patient is found to be legally blind. This would make him eligible for extended benefits such as approved aids for the blind, Talking Book Machine, etc.

A master information and evaluation form is utilized and completed on each patient. A patient may also be assigned to other PMRS therapies, and all treatment is controlled within the limits of his physical and mental tolerance.

Since 1964, seventy patients have been assigned to the Blind Rehabilitation Program. Twenty-nine Neuropsychiatric, thirty-nine General Medical and Surgical, and two Nursing Home Care Unit patients have received instruction in this phase of treatment. Many of these patients are elderly and chronically ill with multiple diagnoses. The extent of treatment of these patients is quite varied and must be limited. Other patients have responded extremely well and have been able to participate in all phases of treatment. Several patients who were considered candidates for intensive instruction were transferred to the VA Hospital, Hines, Illinois.

The following areas of training are given at Togus. Patients receive training in all thirteen areas, and the hospital staff and volunteers are given training in categories one through eight. Patients with remaining vision wear a blindfold during periods of instruction. A blindfold is also worn by the staff and volunteers during part of their training.

1. Use of a sighted guide.
2. Travel in a familiar area.
3. Direction taking.
4. Use of a Braille watch and clock, and telephone.
5. Identification of money and clothing.
6. Eating techniques.
7. Long Cane technique (both indoor and outdoor travel).
8. Ascending and descending stairs.
9. Exploration of work areas.
10. Reading and writing Braille and typing (through the cooperation of Educational Therapy and hospital volunteers).
11. Physical conditioning and prevention of deterioration.
12. Recreational activities.
13. Occupational Therapy (exploratory vocational and avocational).

Various types of aids are made available to the patients. These include Braille watches and clocks, writing guides, electric razors, recreational games including Braille and jumbo print playing cards, Braille and large numbered Bingo cards, etc. Some patients have received special equipment which includes tape recorders, typewriters and Braille writers.

There is a "team approach" used in the treatment of a blind patient and this includes the cooperation of the following services at Togus: Social Work, Prosthetic and Sensory Aids, Psychology, Eye, Ear, Nose and Throat, Vocational Counseling and Adjustment, the ward personnel, and therapists of the Physical Medicine and Rehabilitation Service. The Division of Eye Care and Special Services of the State of Maine Department of Health and Welfare also provides valuable service and equipment for our patients.

The Library at the Perkins School for the Blind, Watertown, Massachusetts, provides a wide variety of recordings for use with the Talking Book Machines.

A ten-hour course in Blind Orientation and Mobility Procedures is given periodically throughout the year. This course is opened to all hospital services including service organizations and voluntary organizations. Certificates of training are presented to each participant upon completion of the course.

The Physical Medicine and Rehabilitation Service maintains its own library of reference material for blind rehabilitation. This literature is available to members of the entire hospital staff.

The Beacon Club is a socially oriented organization for the blind and visually handicapped patients. The Club meets on the first Thursday of each month with refreshments and entertainment being provided by members of the Voluntary Service.

The benefits to the patients and the orientation of people in the paramedical and community services have proved the importance and value of the training of the blind patient. The psychological and emotional responses have helped many, despite their irreversible organic changes, in their resocialization, improved adjustment and independence.

The workers who have participated have commented on the personal satisfaction and the value the course has provided them in the appreciation and the treatment of the blind patient. The goal is to train many individuals in this important phase of rehabilitation so that not only the veteran will benefit, but also the blind and visually handicapped in the community.

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Maine Heart Association Notes
20 Winter Street, Augusta, Maine

Treatment of Hypertension

HARRIET P. DUSTAN, M.D.*

Hypertension shortens life. Even the so-called benign hypertension causes premature death or disability and can scarcely be looked upon as benign. Considering that hypertension is potentially lethal, the question arises as to whether sustained reduction of arterial pressure prolongs life. There are two answers to this question: an unqualified "yes" and a "maybe," depending on whether reference is make to the complications of arteriolar disease or those of atherosclerosis. The most frequent results of hypertensive vascular disease — the term used for the arteriolar disease — are cardiac failure and malignant hypertension. In both instances blood pressure reduction is life-saving providing, of course, that in the malignant hypertensive renal function is still adequate to sustain life. Clinical experience also indicates that good blood pressure control in hypertensive patients without these complications will prevent their occurrence. In contrast, the effects of antihypertensive treatment on the complications of atherosclerosis are not so clear as on those of hypertensive vascular disease, and here the "maybe" answer has to be given. The equivocation in this answer comes because antihypertensive drug treatment has not been used over a long enough period of time to assess its effects on the complications of atherosclerosis that so frequently accompany hypertension. However, there is some evidence which suggests that strokes, at least, occur less frequently in treated patients.

From the foregoing, the goals of antihypertensive treatment can be stated as: 1) to reduce arterial pressure to normal or as near normal as possible, 2) to prevent the progression of arteriolar disease and control its complications if they are present, and 3) to prevent the development of premature atherosclerosis — or at least to prevent or postpone the development of its complications.

There are a variety of ways to treat hypertension effectively. Some are specific in that they eliminate or block a pressor mechanism and thus reduce arterial pressure to normal. Others can be called nonspecific because, although hypertension is greatly lessened, arterial pressure does not become normal. The treatments which in my opinion are specific are both surgical and medical. In a young patient with renal arterial stenosis, a successful operation — either a revascularization procedure or nephrectomy — usually completely eliminates the hypertension. In a substantial number of patients with pheochromocytoma, primary aldosteronism and coarctation of the aorta similar results are achieved by operative treatment. Certain drug treatments also achieve complete normalization of arterial pressure. Thus, in patients with primary aldosteronism, administration of spironolactone eliminates hypertension as surely as does operative removal of the tumor; and in patients with increased activity of the beta-adrenergic component of the sympathetic nervous system, use of a beta-blocking drug such as propranolol not only abolishes the symptoms but also reduces arterial pressure to completely normal levels.

The experience with these "specific" treatments is striking because such results are usually not achieved when the pressor mechanism is not approached directly. For example, contrast the blood pressure reduction achievable by successful operative treatment in a patient with renovascular hypertension with the result produced in the same patient by a drug, like alpha methyl dopa, that suppresses sympathetic vasomotor activity. In the former instance, the operation eliminates the pressor factor (s), while in the latter drug treatment lessens the hypertension but does not eliminate it. The operative treatment is specific, while the drug treatment is nonspecific or empiric.

The fact that most drug treatment of hypertension is empiric is not to say that it is unsuccessful, because substantial reductions in arterial pressure can usually be achieved. There are a number of drugs available which are effective and, for the most part, reasonably easy to take. Two types are most commonly used — oral diuretics and drugs that suppress the activity of the sympathetic nervous system through effects on production, storage or release of the neurotransmitter, norepinephrine. The former group includes chlorothiazide and its derivatives, as well as ethacrynic acid and triamterene; the latter comprise ganglion-blocking drugs, reserpine, guanethidine, alpha methyl dopa and pargyline. Not included in these two groups is hydralazine, which seems to act directly on the arterial wall. The anti-aldosterone drug, spironolactone, has value as nonspecific treatment when used to combat the potassium losing effects of chlorothiazide diuretics.

When used in adequate doses, these drugs usual-

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Prepared by the Maine Heart Association for this Journal.

ly achieve good blood pressure control. When more than one drug is used, combination tablets are not the best way to administer the medication because there is need to individualize the dose of each drug. The most frequent combination of drugs is an oral diuretic with another type because usually there is a synergistic effect on blood pressure reduction — the combination achieving a better result than would be expected from purely additive effects of the two drugs. Not more than one type of chlorothiazide diuretic should be given in a treatment regimen, and, also, there is no evidence that giving more than one type of adrenergic-blocking drug — such as combining guanethidine with methyl dopa — adds any benefit.

When it is necessary to reduce blood pressure rapidly, as in patients with cardiac failure, intracerebral bleeding or hypertensive encephalopathy, good results can usually be achieved by the potent peripherally-acting sodium nitroprusside or diazoxide given intravenously. More readily available, but less potent, are preparations of reserpine, hydralazine, methyl dopa, and ganglion-blocking drugs suitable for parenteral administration.

One crucial question in the long-term treatment of hypertension concerns how to judge the effect of treatment. Actually, use of office pressure measurements is usually unsatisfactory, but for certain patients there is no other way. However, many patients can learn to make their own measurements, and this provides a daily record of responses and allows for judicious adjustment of doses whenever indicated. One mistake that many clinicians make is failure to obtain a good pre-treatment arterial pressure record, and this difficulty can be obviated by use of home readings. The technique is easy to learn, and the measurement is no more difficult to carry out than estimation of urinary sugar — information considered a must in the treatment of diabetes.

With home readings, the physician has the advantage of judging the effects of treatment in two situations rather than one because he additionally obtains office readings when the patient visits him. The more detailed record of treatment response that is available the better can the treatment be managed.

In some patients with hypertension of unknown cause, use of non-specific drug treatments detailed above reduces arterial pressure to normal just as specific treatments do in patients with known types of hypertension. Such responses show that each type of treatment can be specific when properly chosen; the current problem is that, for the most part, there is no sure way to make the proper choice. Currently, the challenge of investigation is to learn enough about the mechanisms of hypertension and how they are interrelated so that specific, rather than empiric, treatments can be given to each hypertensive patient.

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See Clinical Considerations section on last page...

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Important Precautionary Note Patients receiving treatment with GARAMYCIN Injectable (gentamicin sulfate injection) should be under close clinical observation because of the toxicity associated with the use of the drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with preexisting renal damage, treated with GARAMYCIN Injectable for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with preexisting renal damage.

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Pathogens	Percentage of sensitive strains Number of strains tested			Antibiotics*				
	Garamycin	Kanamycin	Cephalothin	Cephaloridine	Ampicillin	Colistimethate	Chloramphenicol	Tetracycline
Klebsiella pneumoniae	99.5% 962	84.7% 992	86.2% 995	76.1% 67	32.7% 1,020	96.3% 640	82.9% 1,028	77.1% 1,026
Aerobacter aerogenes	95.9% 2,739	86.1% 2,818	53.5% 2,985	58.8% 1,514	22.7% 3,066	88.6% 2,603	85.8% 3,071	67.8% 2,981
Klebsiella aerobacter group	98.8% 566	83.9% 547	66.1% 522	60.5% 276	28.0% 553	89.5% 560	86.2% 587	62.8% 433
Klebsiella, all others	92.7% 2,944	83.3% 3,186	77.4% 2,976	67.5% 627	13.5% 2,883	95.0% 2,105	81.6% 3,212	70.6% 3,063
Pseudomonas aeruginosa	91.6% 4,528	29.8% 4,460	6.6% 4,418	6.6% 1,279	6.0% 4,360	91.3% 3,852	26.9% 4,608	26.4% 4,404
Proteus, indole-positive	91.8% 1,031	85.8% 1,062	39.9% 981	54.1% 364	40.2% 1,042	10.3% 758	76.1% 1,096	42.1% 1,051
Proteus mirabilis, indole-negative	94.9% 3,272	90.1% 3,378	83.1% 3,290	77.5% 975	78.0% 3,274	8.8% 2,634	85.9% 3,469	26.8% 3,278
Proteus, unspecified	96.2% 1,335	85.8% 1,371	71.7% 1,434	70.0% 647	64.7% 1,435	11.2% 1,233	76.0% 1,421	22.4% 1,298
Escherichia coli and all other *Escherichias*	96.4% 12,557	91.4% 12,818	87.8% 12,686	88.8% 4,251	74.6% 12,899	95.4% 10,623	94.1% 13,086	70.0% 12,559
Paracolobactrum, all	93.4% 303	88.9% 325	62.0% 305	74.2% 62	43.8% 340	80.9% 215	87.1% 350	72.6% 340
Coliform bacteria	99.0% 593	91.2% 649	81.5% 637	66.7% 21	52.7% 624	95.6% 607	91.6% 678	76.1% 637
Totals	95.1% 30,830	80.5% 31,606	65.3% 31,229	68.1% 10,083	50.3% 31,496	75.8% 25,829	79.7% 32,606	56.5% 31,070
Gram-positive (included for consistency with Package Insert, not an approved indication)								
Staph—*S. aureus*, coagulase-positive	97.4% 1,548	88.8% 1,458	97.7% 2,050	98.7% 636	61.1% 1,559	20.4% 628	94.4% 2,123	83.7% 1,966
Staph—*S. aureus*, unspecified	99.3% 993	92.8% 902	98.1% 1,289	95.3% 213	45.8% 1,153	29.3% 116	96.4% 1,427	82.3% 1,360

*Adapted from a three-month, nationwide hospital audit by R. A. Gosselin and Co., Inc., Dedham, Massachusetts (mid-May to mid-August, 1969).[8]
Antibiotics with significant gram-negative spectra are included. Organisms are listed as reported by laboratory.
Sensitivity testing was done by the disc method, a generally reliable test in the hospital setting. It should be noted, however, that the results with GARAMYCIN were somewhat higher than the results reported where the tube dilution technique was used. (See Clinical Considerations section which follows.) The concentration of the GARAMYCIN disc was 10 mcg.
Whereas standard testing methods were used by all hospitals, it is acknowledged that in a survey of this kind considerations such as differences in methodology are possible sources of error. The comparative percentage-sensitivity results derived from a survey of this kind are, therefore, not absolute. One should keep in mind also that the proper selection of an antibiotic is based not only on susceptibility testing but on relative toxicity and other clinical considerations as well.
It is felt, nonetheless, that the broad scope of the survey and the extreme care in data collection and tabulation permit a conclusion that the results are *generally* representative of current nationwide antibiotic sensitivity patterns.

Injectable Garamycin®
brand of **gentamicin sulfate injection**

See Clinical Considerations section on last page...

Injectable Garamycin®

brand of gentamicin sulfate injection

Schering

ADULT DOSAGE GUIDELINES

See definitive prescribing information in Package Insert.

Patients with Normal Renal Function

Total Daily Dose (administered in two, three, or four divided doses)			
Urinary Tract Infections (due to susceptible strains of gram-negative bacteria)†	**Less Severe** 0.8-1.2 mg./kg. for 7-10 days	**Resistant/ Moderately Severe** Larger doses or additional antibacterial therapy should be considered in severe urinary tract infections or in resistant cases involving the renal parenchyma or anatomic anomaly.	**Serious/Life-Threatening** up to 5 mg./kg.
Other Infections including bacteremia, infected surgical wounds, severe soft tissue infections, and respiratory tract infections (due to susceptible strains of gram-negative bacteria)	3 mg./kg. for 7-10 days		

†Alkalinization of the urine may be a useful therapeutic adjunct.

Patients with Impaired Renal Function

To minimize the risk of ototoxicity in patients with impaired kidney function, only the first dose should be that normally recommended. Each subsequent dose should be half or less of that recommended for patients with normal renal function, depending upon the degree of renal impairment.

In patients with renal failure who are undergoing 14-hour hemodialysis twice weekly, administration of 1 mg./kg. GARAMYCIN Injectable at the end of each dialysis period has been suggested.

Clinical Considerations

Indications: GARAMYCIN Injectable is clinically effective in infections due to susceptible strains of gram-negative bacteria, including *Pseudomonas aeruginosa*, and species of indole-positive and indole-negative *Proteus*, *Escherichia coli*, and *Klebsiella-Aerobacter*. Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose. If the susceptibility tests indicate that the causative organism is resistant to gentamicin sulfate, other appropriate antibiotic therapy should be instituted.

IN VITRO INHIBITION OF CLINICALLY IMPORTANT BACTERIA BY GENTAMICIN SULFATE (TUBE DILUTION STUDIES)

BACTERIA	No. of Strains Tested	No. of Strains (%) Inhibited by: 4 mcg./cc. or less		8 mcg./cc. or less*		No. of *In Vitro* Studies
Staphylococcus aureus	1,210	1,200	(99%)	1,206	(99%)	11
Pseudomonas aeruginosa	885	771	(87%)	828	(93%)	16
Escherichia coli	836	736	(88%)	779	(93%)	11
Indole-positive and indole-negative *Proteus* species	477	210	(44%)	358	(75%)	12
Klebsiella-Aerobacter species	292	205	(70%)	231	(79%)	10

*Number of strains (%) of gram-negative bacteria inhibited by 10 mcg./cc. or less are as follows: *Pseudomonas aeruginosa*, 828 (93%); *Escherichia coli*, 792 (95%); *Proteus* species, 393 (82%); *Klebsiella-Aerobacter* species, 284 (97%). From same studies as above.
Source: Package Insert

This drug should be limited to the treatment of serious infections caused by gram-negative bacteria, particularly *Pseudomonas aeruginosa*, *Proteus* and other susceptible organisms, with due regard for relative antibiotic toxicity. Therefore, the drug should be considered for use against gram-negative: 1. Bacteremia; 2. Infected surgical wounds; 3. Severe soft tissue infections, including burns complicated by sepsis; 4. Respiratory tract infections; and 5. Selected cases of urinary tract infection.

Contraindications: GARAMYCIN Injectable is contraindicated in individuals with a history of hypersensitivity or toxic reactions to gentamicin.

Warnings: Patients receiving treatment with GARAMYCIN should be under close clinical observation because of the toxicity associated with the use of this drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with pre-existing renal damage, treated with GARAMYCIN Injectable usually for longer periods or with higher doses than recommended

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with pre-existing renal impairment. Kidney function diminished by infection of the upper urinary tract may, however, improve during effective treatment with GARAMYCIN Injectable.

Concurrent administration of potentially ototoxic drugs such as streptomycin and kanamycin or of potentially nephrotoxic drugs such as polymyxin, colistin, and kanamycin with gentamicin sulfate has not been shown to afford any clinical advantages and, moreover may result in additive toxicity. Monitoring of vestibular, cochlear, and renal function will provide guidance for therapy in such cases.

Precautions: In patients with impaired renal function in whom serious infection develops, serum concentrations of the drug may rise, with consequently increased risk of ototoxicity. In these patients or in those in whom recommended dosage or duration of therapy must be exceeded as a life-saving measure, routine studies of kidney function should be performed when possible. These may be supplemented by evaluation of the vestibular and auditory function and measurement of serum concentration of the drug when feasible. Serum concentrations of gentamicin should be maintained below the range of 10-12 mcg./ml. to reduce risk of ototoxicity.

Ordinarily, treatment should not be given for more than 7 to 10 days or be repeated unless required for serious infection not responsive to other agents.

As with other antibiotics, treatment with GARAMYCIN Injectable may occasionally result in overgrowth of nonsensitive organisms. If superinfection occurs, appropriate therapy is indicated.

Safety for use in pregnancy or the potential for fetal ototoxicity or nephrotoxicity have not been established. Studies in pregnant animals have not revealed teratogenic or ototoxic effects in the fetus. GARAMYCIN Injectable should not be used in pregnant patients or in women of childbearing age unless its use is deemed advisable by the physician.

Adverse Reactions: The overall incidence of ototoxicity considered related to treatment with GARAMYCIN Injectable was 2.8 per cent (16 of 565 patients). Contributory factors (two or more factors were relevant to most patients) were as follows: 10 had azotemia, 10 received a total of 1 gram or more of the drug, 7 had recently received other potentially ototoxic antibiotics (streptomycin or kanamycin), and 5 were over 60 years of age. Six also had decreased high-tone hearing acuity, which returned to or toward normal in the 4 patients retested.

Analysis of BUN data indicated that 4 (2%) of 172 patients showed increases in BUN that were probably related to treatment with GARAMYCIN Injectable. Of 20 increases probably or possibly related to treatment, 7 were reversible, 9 occurred in terminal patients, and 4 had no follow-up.

Other adverse reactions associated with treatment were one instance each of urticaria, decreased hematocrit, and reversible depression of granulocytes with normal bone marrow. Other rarely reported and possibly treatment-related adverse reactions were anemia, increased reticulocyte count, rash, purpura, drug fever, hypotension, convulsions, twitching, salivation, nausea, vomiting, increased transaminase activity (SGOT or SGPT), increased serum bilirubin, decreased serum calcium, and joint pain.

Packaging: GARAMYCIN Injectable, 40 mg./cc., 2-cc. multiple-dose vials, for intramuscular administration.

References: (1) Brayton, R. G., and Louria, D. B.: Gentamicin in gram-negative urinary and pulmonary infections, Arch. Int. Med. *114*:205, 1964.* (2) Louria, D. B.; Young, L.; Armstrong, D., and Smith, J. K.: Gentamicin in the treatment of pulmonary infections, J. Infect. Dis. *119*:483, 1969. (3) Cox, C. E.: Gentamicin, a new aminoglycoside antibiotic: Clinical and laboratory studies in urinary tract infections, J. Infect. Dis. *119*:486, 1969. (4) Groll, E.: Clinical experience with gentamicin, data from 12 German clinics, in Gentamicin: First International Symposium, Paris, January 1967, Lucerne, Essex Chemie AG, pp. 121-128.* (5) Jackson, G. G.: Laboratory and clinical investigation of gentamicin, *ibid.*, pp. 62-74. (6) Medeiros, A. E.: Discussion, J. Infect. Dis. *119*:533, 1969. (7) Polk, H.: Discussion, J. Infect. Dis. *119*:529, 1969. (8) Three-month, nationwide hospital audit by R. A. Gosselin and Co., Inc., Dedham, Massachusetts (mid-May to mid-August, 1969).

*Dosage in this investigational study was less than now recommended in Package Insert.

For more complete prescribing details, consult package insert or Physicians' Desk Reference. Schering literature is also available from your Schering Representative or Medical Services Department, Schering Corporation, Union, New Jersey 07083.

AHFS CATEGORY 8:12.28 S-029

AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

Gallup Study Shows Increase in Medical Checkups

ATLANTA, GA. — A nationwide Gallup study has shown a gradual increase in the percentage of Americans who get medical checkups, it was announced recently by William B. Lewis, Chairman of the Board of the American Cancer Society.

The findings were presented to the Public Education Committee of the Society whose National Board of Directors is meeting here at the Marriott Motor Hotel. The study also showed a slowing down of the rate of increase of those who went for specific cancer tests.

Among the important facts brought to light were:

— A modest gain in the percentage of those who ever went for a complete physical checkup although they were feeling well — from 55 percent in 1961 to 57 percent in 1963 to 62 percent in 1970. Larger gains were scored in the South and West than in the East and Midwest, and among lower income and less educated people.

— Sizable gains in the percentages of those who have heard of the various cancer detection tests. Here women's familiarity with the Pap test for cervical cancer showed the greatest gain — up from 59 percent in 1961 to 77 percent in 1963 to 90 percent in 1970. But just 53 percent said they'd had the Pap test, compared to 48 percent in 1963 and 30 percent in 1961. This indicated lack of action by many of those who knew of the tests.

Slight increases in those who ever had various cancer detection tests, but a slowdown in the rate of growth. For most of these tests — skin, proctoscopy, breast examinations and Pap smears — there were two to five percentage point increases from 1963 to 1970.

The Gallup study for the American Cancer Society was conducted in March 1970 and was based on a cross-country sample of 1,573 adults consisting of 785 men and 788 women.

In addition to the gains among women who had heard of the Pap tests, nine out of ten had heard of breast self-examination. About one out of two women had done BSE at some time and 34 percent had done it in the past year. Most of those who had ever done it continued to do so in the past year (42 out of 49 percent), indicating that when a woman is persuaded to try BSE once she will most likely continue the practice.

On the other hand, the study showed that those women who did BSE varied the frequency with only one out of seven performing BSE at the recommended monthly interval. Moreover, the frequency rises somewhat among women in the 35-49 age bracket, is higher in the West, is lowest among black women, with 33 percent having done it in the past year, compared to 44 percent of white women.

Among those who had gone for checkups, answers to the question, "Why did you go on that occasion?" were:

"I have to have periodic checkups for birth control pills" — a 23-year-old woman in Los Angeles, Calif.

"My back was hurting" — a 67-year-old man in El Dorado Springs, Missouri.

"Because of pressure from the family. They felt I should have cancer tests" — a 66-year-old women in South St. Paul, Minn.

Several answers to the question "Could you tell me why you first happened to have the Pap test?" were:

"My doctor suggested it every year" — a 31-year-old in Staten Island, New York.

"Publicity of the Cancer Society" — a 55-year-old in DeWitt, Missouri.

Insofar as ACS programs are concerned, Mr. Lewis said, perhaps more attention should be paid to possible "environmental restraints and barriers" that may have to be removed to persuade "a hard core of resistors to have cancer tests."

American Cancer Society News Service Release.

County Society Note

CUMBERLAND

A meeting of the Cumberland County Medical Society was held on April 16, 1970 at the Crescent Beach Inn in Cape Elizabeth, Maine. There were seventy members and guests in attendance. This meeting of the Cumberland County Medical Society was a combined meeting with the staff of the Pineland Hospital.

Following a social hour and dinner, the President, George F. Sager, M.D. introduced C. Philip Lape, M.D., President of the staff of the Pineland Hospital, and Dr. Lape introduced the speaker of the evening, Dr. Richard Steinman.

Dr. Steinman spoke on the impact of social change upon the physicians' work. He stressed that physicians must become willing partners to change. It was a most interesting and stimulating talk. Dr. Steinman graciously answered questions following the formal presentation.

At 9:00 p.m., the business meeting of the Cumberland County Medical Society was called to order by Dr. Sager. It was voted the minutes of the previous meeting be dispensed with.

It was announced that the report of the Priority Committee undertakings have been processed and will be distributed to the membership in large manila envelopes. The membership of the Cumberland County Medical Society was urged to consider the reports carefully as they contained widesweeping suggestions for change and improvement. The report is to be dealt with at the next meeting in some detail.

It was urged by the membership that an agenda be prepared for the May 21st meeting. This was agreed to by President Sager and will be prepared by the Executive Committee.

DOUGLAS R. HILL, M.D., *Secretary*

News, Notes and Announcements

Shriners Offer Unusual Burns Service

The Shriners Burns Institute of Boston is a small, thirty-bed hospital for the care of children of fifteen years or less. Admission is dependent on the need of the patient and the availability of beds. All burned children are welcome. Medical staff is shared with the Massachusetts General Hospital.

For the acutely burned child needing immediate care, the referring physician should contact the Institute directly (phone: 617-722-3000). He should state that he has a patient needing emergency admission and ask to speak to the Admitting Officer. Patients sent by plane will be met at the airport by ambulance supplied by the Institute. Shrine applications are included in the admitting procedure.

For the child needing reconstructive or restorative surgery and rehabilitation as a result of previous burn injuries, applications are available from Shrine Temples, individual Shriners or from the Shriners Burns Institute, 51 Blossom Street, Boston, Mass. 02114.

Professional Publications and Films on Arthritis Available to Members of the M.M.A.

An up-to-date listing of Arthritis Foundation-produced professional publications and films can now be obtained from the Maine-Pine Tree Chapter of The Arthritis Foundation.

The publication lists six films and scores of publications which are available to members of the Maine Medical Association for their own use as well as where appropriate for distribution to arthritic patients.

Copies of the list are free for the asking from The Arthritis Foundation, Maine-Pine Tree Chapter, P. O. Box 333, Bath, Maine 04530.

State of Maine Board of Registration of Medicine
Secretary — George E. Sullivan, M.D.
Waterville, Maine

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ecautions: Drowsiness, anorexia, slight gasc distress can occur. In excessive drowsiss, consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat betahemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

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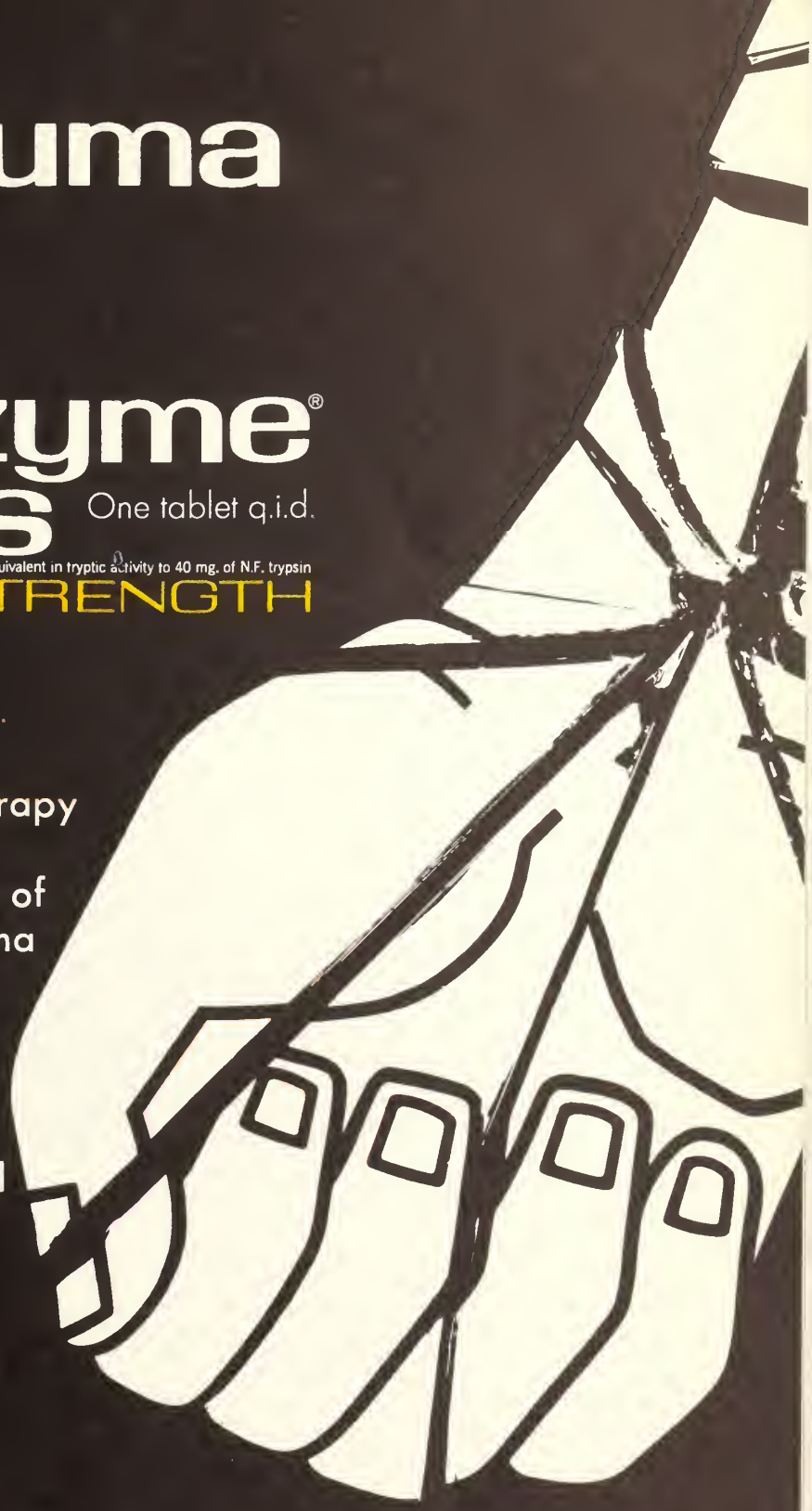

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Precautions: It should be used with caution in patients with abnormality of the blood clotting mechanism such as hemophilia, or with severe hepatic or renal disease. Safe use in pregnancy has not been established.

Adverse Reactions: Adverse reactions with ORENZYME have been reported infrequently. Reports include allergic manifestations (rash, urticaria, itching), gastrointestinal upset and increased speed of dissolution of animal-origin surgical sutures. There have been isolated reports of anaphylactic shock, albuminuria and hematuria. Increased tendency to bleed has also been reported but, in controlled studies, it has been seen with equal incidence in placebo-treated groups. (See Precautions.) It is recommended that if side effects occur medication be discontinued.

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References: 1. Gardner, H. L.: J. Miss. M.A. 8:529, 1967. 2. Porter, P. S., and Lyle, J. S.: Arch. Dermat. 93:402, 1966. 3. Walsh, H.; Hildebrandt, R. J., and Prystowsky, H.: Am. J. Obst. & Gynec. 93:904, 1965. 4. Vaginitis and the Pill: J.A.M.A. 196:731, 1966. 5. Guerriero, W. F.: South. M.J. 56:390, 1963. 6. Seelig, M. S.: Am. J. Med. 40:887, 1966. 7. To-day's Drugs, New York, Grune & Stratton, Inc., 1965, p. 316. 8. Gray, L. A., and Barnes, M. L.: Am. J. Obst. & Gynec. 92:125, 1965. 9. Salerno, L. J.; Ortiz, G., and Turkel, V.: Vaginitis: A Diagnostic and Therapeutic Approach, Scientific Exhibit, presented at the 115th Annual A.M.A. Convention, Chicago, Illinois, June 1966. 10. Walsh, J. C.; Sheffery, J. B., and Wilson, T. A.: Med. Ann. D.C. 37:358, 1968. 11. Nugent, F. B., and Myers, J. E.: Pennsylvania Med. 69:44, 1966.

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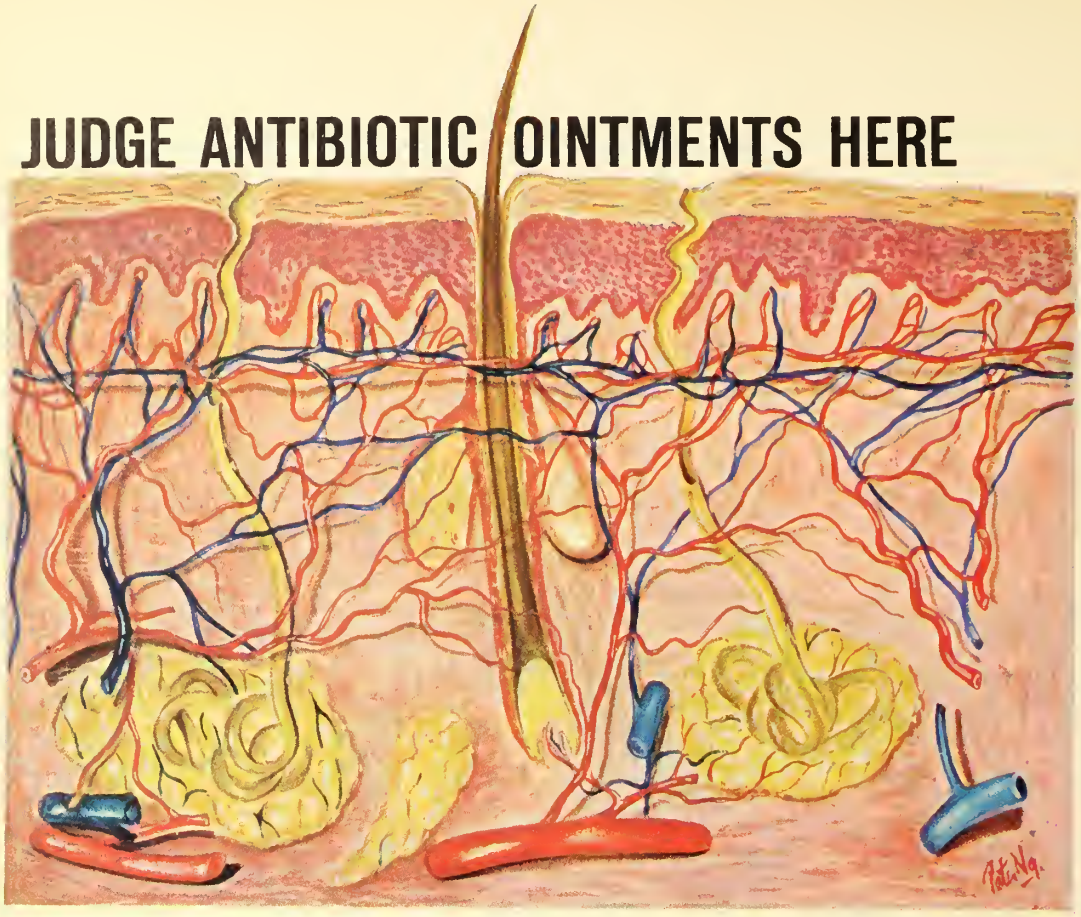

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1. Kannel, W.B., *et al.*: *Circulation* 35:734, 1967.
2. Thomas, H.E., Jr., *et al.*: *Med. Times* 95:1099, 1967.
3. Albrink, M.J., in: Beeson, P.B. & McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Phila.: W.B. Saunders Co., 1967.

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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VOLUME 61 | AUGUST 1970 | NUMBER 8

Augusta General Hospital Number

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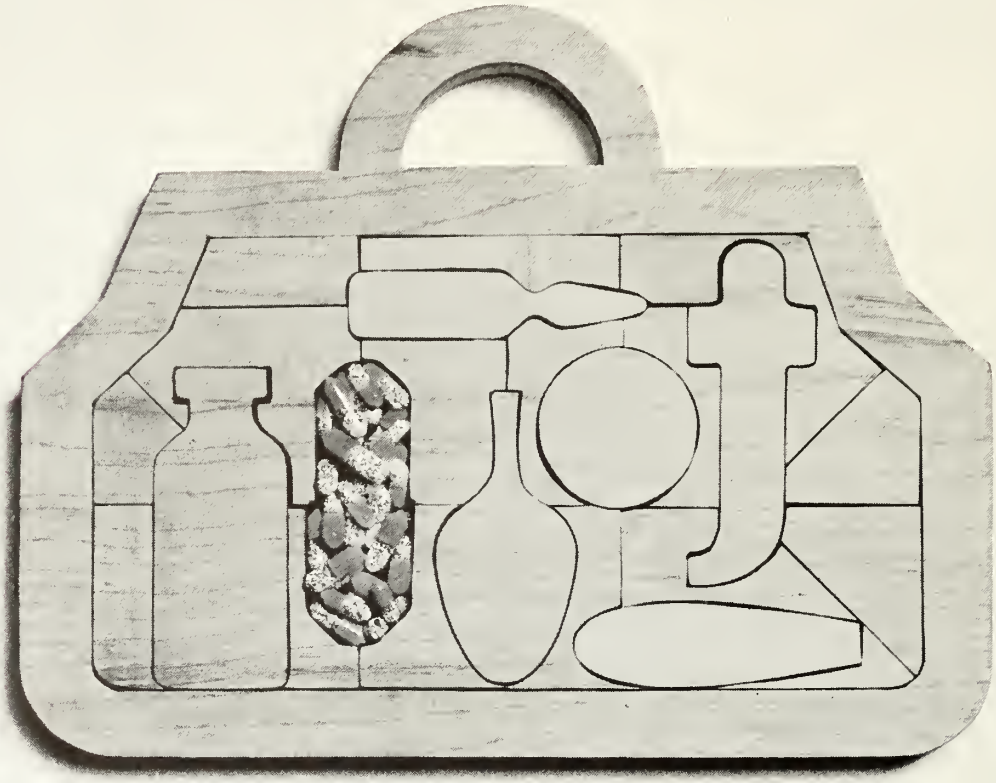

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* PATRICIA A. BERGERON, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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Precautions: Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects: Gastrointestinal system – anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin – maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney – rise in BUN, apparently dose-related. Transient, reversible, nephrogenic diabetes insipidus with excessive thirst and polyuria (rare). Hypersensitivity reactions – urticaria, angioneurotic edema, anaphylaxis. Teeth – dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy. Demethylchlortetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.

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Mammography in the Community Hospital

DEMITRIOS NIKOLAIDIS, M.D.* and FRANCIS J. O'CONNOR, M.D., F.A.C.R.**

Cancer of the breast is the most common of major cancers and numerically the most lethal of all malignant diseases affecting the American female population. One of every 19 women born will develop this disease. It is the leading cause of death in women 40 to 44 years of age. Breast cancer incidence and mortality rise sharply during the reproductive years, then continue to rise postmenopausally but at a slower rate. Breast cancer incidence prior to age 55 has increased about 45% since 1935 while above age 55 has remained constant.

The diagnosis of breast cancer has multiple ramifications. There is first the patient without a lump. The physician must always bare in mind the frequency of cancer of the breast. The general practitioner has the opportunity to examine the breast and so does the internist, the surgeon and the obstetrician-gynecologist. Second is the patient with a breast lump. Here is a problem to be solved by one experienced in the diagnosis of neoplastic diseases of the breast, both benign and malignant. A standard examination inspection for patients including the sites of lymphatic spread and the opposite breast are the principle ways of evaluating this problem. The issue of adequacies and inadequacies of clinical examination of the breast within the context of experience gained in the breast cancer search is debatable.

The breast is most accessible to clinical examination but physicians were missing 25% of the relatively advanced breast cancers on initial examination according to Robert L. Egan. Mammography has played a tremendous role in the problems of early detection of cancer of the breast. It was first introduced in 1956. At that time, there was a high incidence of the disease and, a very low 10-year salvage rate.

*Associate Radiologist, Department of Radiology and Nuclear Medicine, Augusta General Hospital, Augusta, Maine 04330.
**Director of the Department of Radiology. Augusta General Hospital, Augusta, Maine 04330.

Physical examination is the mainstay of breast cancer detection and, in expert hands, can be 70% accurate as demonstrated by Gilbertsen Day, et al. However, when the clinician supplements his skills with proficient mammography, an accuracy of 90% can be achieved.

Mammography is a very reliable means of detecting breast cancer prior to signs and symptoms. It is a three dimensional study of both breasts and surrounding tissues, invaluable to the clinician and the pathologist. Mammography can reveal lesions as small as 5 mm. and can demonstrate the microcalcifications seen in duct cell carcinomas that cannot be palpated. The clinical examination is particularly inadequate in the detection of breast cancer which is demonstrated only by calcifications on x-ray. Louise Venet has reported that when one correlates the radiologic findings with those of clinical examination, only 3 of the 15 with calcifications radiologically are definitely palpable clinically on re-examination. When the radiologic finding was that of a mass, 19 out of 25 were palpable on re-examination. Mammography is of course most helpful in patients with large breasts.

Mammography can be a source of rapport between the physician and patient. There is a certain magic appeal to x-ray and the patient feels that something special is done for her. Consequently, the action and concern of the physician will be noted by the family and members of the community. A new atmosphere will develop in the community, more cures will beget more interest and care. At Emory University Hospital, Atlanta, Georgia, where such a rapport has been established, 80% of the patients operated are in Stage 0 or Stage 1 breast cancer.

Screen surveys of groups of women have been done using mammography with impressive results. Witten and Thurber examined 5,000 women hospitalized for reasons other than breast complaints. They found 8 unsuspected cancers, an incidence of 1.6 in 1.000. The surgical specimen in each incident was free of spread. Wolfe

TABLE 1

RESULTS OF MAMMOGRAPHY AT THE AUGUSTA GENERAL HOSPITAL

Number of Mammograms	*Malignancies*	*No axillary metastasis*	*Microcalcifications*	*Negative Clinical Examinations*	*Not Diagnosed as malignancies on mammograms*
701	42	24	9	2	7

surveyed 3,891 women and found 16 cancers, an incidence of 4.11 per 1,000. One malignancy was only 5 mm. in diameter. No metastasis was present in 14 of the 16 cancers removed surgically. Stevens and Weigen screened 1,223 asymptomatic women over 40 years of age and found 8 cancers. These were not suspected clinically and there was no associated axillary metastasis. According to Dr. Egan, there is conclusive evidence that by mammography many breast cancers can be detected as long as two years prior to clinical recognition. However, en masse mammographic screen studies such as these are not feasible. Such a screening program of women over 40 years of age would require approximately 7,000 mammograms per year performed by each already over-loaded radiologist. A better program would include those patients of the high risk group with large breasts. It is well documented that a non-simultaneous carcinoma in the remaining breast following mastectomy is 2 to 7 times more frequent than in the average population. There is an incidence of 1% per year of carcinoma developing in the opposite breast. Mammography survey would seem to have particular application in this group. It has become a routine policy in our cancer management program to get a mammogram at 6 months and then at yearly intervals in those patients with treated carcinoma of the breast.

The senior associate, after spending a week at the Emory University Hospital, Atlanta, Georgia with one of the pioneers of this procedure Dr. Robert R. Egan, was quite convinced that this method was extremely valuable for the early detection of breast cancer. Subsequently, Mammography was introduced and popularized at the Augusta General Hospital at the end of 1966.

The examination includes three views, namely the lateral, craniocaudad, and the axillary view of both breasts. Industrial Kodak M54 film in 10 x 12 inch size is used with a non-screen cardboard holder. The low KV technique in the range from 20 KVP with an extension cone for collimation and a special x-ray tube with beryllium window are used as recommended by Dr. Egan. The films are processed manually and not through an automatic processor. All the patients are seen by the radiologist. The breasts and the lymph node bearing areas are carefully inspected and examined in supine and upright positions and findings are recorded. The patients are asked not to leave the department before the films are seen wet to insure that the films are satisfactory. If necessary, spot films of a particular area of the breast or repeat films of the breast are obtained. Occasionally a medio-lateral projection is of value for medial lesions. This is a lengthy procedure and requires that the patient remains in the department from 45 minutes to an hour. Only when the films are dry are they carefully studied with a bright light of varying intensity and magnifying lens. A report is then sent to the referring physician. In general, the radiologist may be faced with the following:

1. He may see nothing of importance on the x-rays.
2. Diagnosis of a benign process is made.
3. Excisional biopsy may be recommended if the findings are not definitely conclusive.
4. And, finally, a diagnosis of malignancy can be made.

Gradually mammography has been accepted by the staff and an increased number of patients have been referred to the radiology department for mammography. In late 1967, a new pathologist, Dr. James Hayes, and recently Dr. Peter Macomber joined the staff of the Augusta General Hospital, and mammography has become very well accepted. The referring physician, the surgeon, the radiologist and pathologist working as a team have brought about the successful application of this technique. Occasionally mammography may be used on the surgical specimen to aid in localizing for frozen section the area of suspicious malignancy.

A review of seven hundred and one (701) mammograms performed at the Augusta General Hospital up to March 1970 showed that forty-two (42) were found histologically to be related to malignancy. Of the forty-two (42) cases, twenty-four (24) were found at the time of operation not to have metastasis to the axillary lymph nodes. Three (3) were cancers developed in the remaining breast after previous mastectomy. Nine (9) mammograms showed classical fine microcalcifications so typical of the ductal carcinamos. This is very close to Dr. Egan's figure that about 25% of the detectable by mammography carcinomas are presented with the very fine microcalcifications. In seven (7) patients, a diagnosis of malignancy was not made on the mammogram. A review of these cases shows that even in retrospect the diagnosis based on the well-established criteria of malignancy cannot be made except for possibly one which apparently was missed. It is of interest to stress the fact that in all these seven (7) patients, changes of fibrocystic diesease were seen on the mammograms and confirmed by microtissue studies and no axillary metastasis was found.

CONCLUSIONS

1. In our series, one case of unsuspected and clinically undetectable carcinoma was found only by mammography out of seven hundred and one (701) cases. This is not very far from the national rate of 1.6 per 1,000 in the United States of occult breast carcinomas detected in

the surveys in unselected women over 40 years of age. The second case was not included in here since it belongs in the high risk group.

2. The microcalcifications so characteristic of malignancy are, indeed, of great significance and help if detected on the mammograms. Very careful examination of the films, using a magnifying lens and bright light, are a routine necessary part of the examination.

3. Carcinoma can be missed in breasts with extensive fibrocystic disease. It is in this group where excisional biopsy may be very important and most often indicated. A thorough review of the world literature by Davis, Simons & Davis summarized that the breast cancer risk of women with cystic disease of the breast is 2.64 times that of women in general.

4. If, on clinical grounds, malignancy is suspected, even though the mammography is negative for malignancy but a fibrotic stroma is present the surgeon should not hesitate to proceed with a biopsy.

5. Interpretation of mammograms in patients with large breasts or post-menopausal breasts where the adipose tissue is large, is relatively easy and even very small lesions in these patients can be seen and detected early. On the contrary, very small and underdeveloped breasts or very densely glandular breasts are difficult to interpret.

6. Survey mammography, besides not being feasible under the present circumstances, is unlikely to significantly alter the survival statistics relating to breast carcinoma in the United States.

7. Mammographic studies are of greatest benefit in high risk groups such as those who have had previous mastectomy and those with strong family history, and in patients with large breasts where the examination is difficult.

8. Failure of patients and or referring physicians to accept biopsy recommendations by the radiologist may limit the practical usefulness of this method.

9. Patients with the smallest cancers and the fewest metastases to the lymph nodes do have the most favorable prognosis. Emory University breast cancer patients without axillary lymph node metastasis had a 70% 10-year salvage as compared to 29% survivors with positive axillary nodes. This is a very impressive decrease, indicating the value of the team approach to breast cancer with the referring physician, surgeon, radiologist and pathologist.

ACKNOWLEDGEMENT

The authors would like to express their appreciation to Dr. James Hayes, Director of the Department of Pathology, and Dr. Peter Macomber, Associate Pathologist. Without their contribution, this study would not have been possible.

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Vitamin B-12 Injections

A recent directive from the Social Security Administration has informed Carriers of those conditions for which reimbursement may be made for vitamin B-12 injections.

Based on professional medical advice, vitamin B-12 injections are specified therapy for — **Certain anemias:** pernicious anemia; megaloblastic anemias; macrocytic anemias; fish tapeworm anemia. **Certain gastrointestinal disorders:** gastrectomy; malabsorption syndromes such as sprue and idiopathic steatorrhea; surgical and mechanical disorders such as resection of the small intestine, strictures, anastomoses and blind loop syndrome. **Certain neuropathies:** posterolateral sclerosis; other neuropathies associated with pernicious anemia; during the acute phase or acute exacerbation of the following — multiple sclerosis, trigeminal and glossopharyngeal neuralgia, neuropathies of malnutrition and alcoholism, tabes dorsalis, causalgia, postsympathectomy parasthesias, diabetic neuropathies and herpes zoster and other inflammatory neuritides not due to mechanical or traumatic etiology.

No reimbursement can be made for vitamin B-12 injections when given for conditions other than those specified above. — **From Medicare Health Insurance Part B, Box 4629, Portland, Maine.**

T.V. Viewing in Radiotherapy and Continuing Education*

ROBERT F. O'CONNOR, R.T.**

BASIC T.V. SYSTEM FOR USE IN VIEWING PATIENTS RECEIVING HIGH ENERGY RADIOTHERAPY

A simple closed-circuit television system consisting of a television camera, associated cables and television monitor may be used to advantage in viewing patients receiving radiotherapy. The camera should be mounted in a position which will allow viewing of the treatment area and also about half the patient's body. The treatment area should be centered on a television camera. Wall mounts are available to mount the camera. Most have swivel type tripod heads which allow easy movement for positioning of the camera.

In simple systems, there are two cables coming from a television camera. One is the power supply which is 110 volts AC, the normal household current. The other cable is the television video cable, a coaxial cable which is connected between the camera and the television monitor. The television monitor may be mounted in any convenient location and it also has two cables coming from it. One is the 110 volt power supply cable and the other is the video cable from the television camera. The use of a closed-circuit television system allows the technician more freedom than the mirror system generally in use in radiotherapy. With the mirror system, the technician must stand by the door to look through the window and see the patient reflected in the mirror on the wall. With the television system, the technician gets a closer view of the treatment area and patient than can be obtained by mirrors. There is available a remote control zoom system which will permit even closer viewing if necessary. The image on the monitor may be placed conveniently for the radiotherapy technician and will allow the radiotherapy technician to work more efficiently.

OPERATION OF A 3-CAMERA SYSTEM, SPECIAL EFFECTS GENERATOR

Our therapy suite[1] has two treatment rooms, each equipped with a television camera. The two cameras not only allow viewing of radiotherapy patients but also allow the treatment rooms to be used as small television studios for producing educational video tapes. A third high resolution view-finder camera is available as a mobile clinical camera. To operate three television cameras simultaneously, the cameras must all operate from a single synchronous source. The "sync" source provides a "sync" signal which causes the television cameras or televisions vidicon tubes in the cameras to scan the same place at the same time. Television is scanned at a rate of 525 horizontal lines per frame, a frame being one picture and the frame rate is 30 frames per second. A "sync" generator must be used when using more than one camera so that all the cameras used will be in phase. This means that in switching from one camera to another camera the television picture will not "roll" or "break up." The "sync" source is also necessary when using a special effects generator to produce split frame images, fades, lap dissolves and other special effects. In this system, each camera has three cables. One cable is the 110 volt power supply cord; the second is the video picture cable – the coaxial cable; the third is the "sync" cable which is a conglomerate of small conductors. There are two small coaxial cables contained in this large one for the two sync signals, the horizontal sync and the vertical sync. There is another coaxial cable intercom system and a single conductor cable for the "tally" lights which may be used on some cameras to indicate which camera is in use. The two main signal cables, #2 and #3 from each of the cameras run to the special effects generator. (See Fig. 1). From the special effects generator, there are three video cables which run to three small monitors which view the pictures from each of the three cameras. All three of the sync cables from the cameras also connect to the special effects generator. From the special effects generator, a composite video signal is run to a video tape recorder and a final output monitor. Usually the signal runs to a video tape recorder and from the video tape recorder the signal runs to a television monitor.

The special effects generator produces "random interlace" sync, but an optional "2 to 1 interlace" sync generator is available. This generator produces a broadcast quality sync signal.

When producing a video educational program, audio equipment is necessary and should consist of an audio mixer with separate volume control for each input, a number of microphones, depending on the number of participants in an interview presentation. A music background may also be connected to the audio mixer from a tape recorder or a record player. The signal from the audio mixer runs to the video tape recorder.

This audio-video system has been designed so that it is almost a one-man operation. In this system, the two

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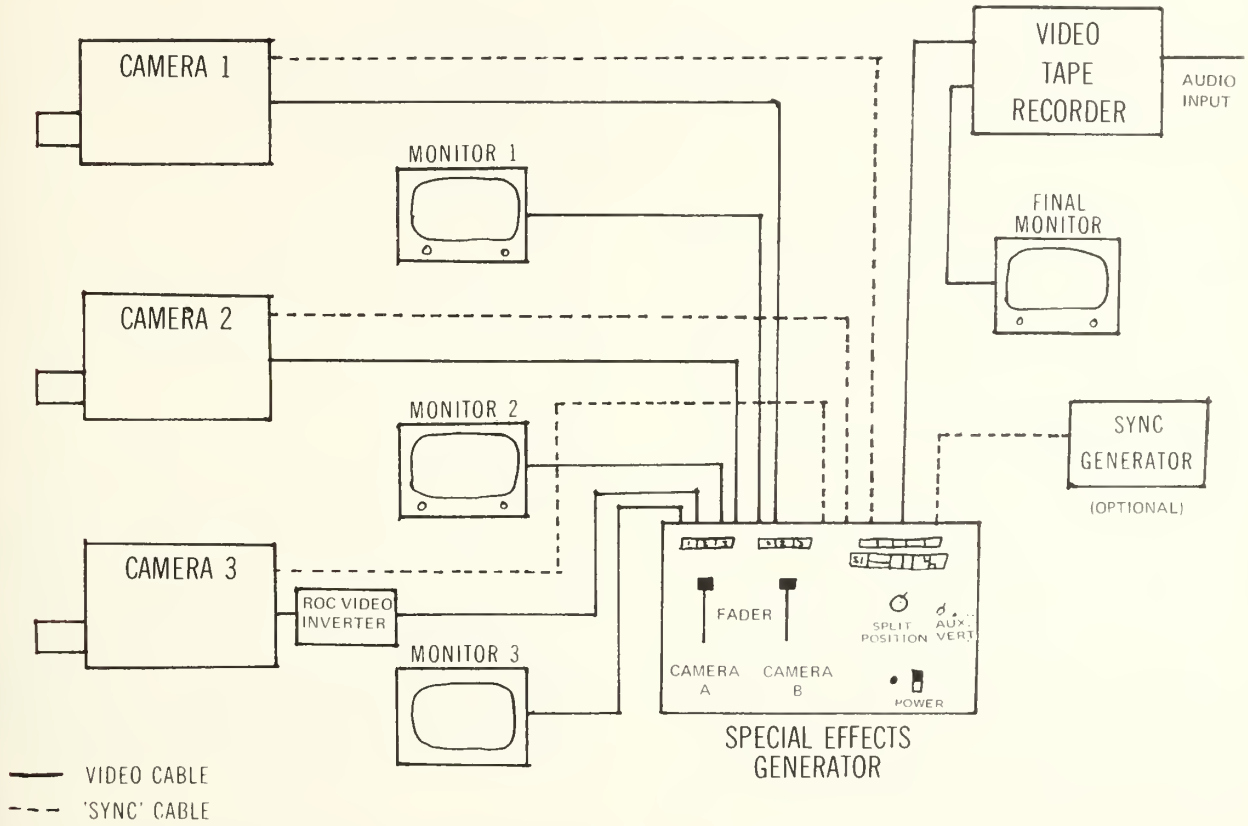

Fig. 1

cameras used for viewing the patients are nonview finder or simply surveillance cameras mounted on tripods and directed at the participants at an interview. The third camera, the view finder camera, should ideally be operated by a separate cameraman. This camera may be used for closeups of the speakers while the two surveillance cameras may be used simultaneously as a tilter in order to place the name of the participant in the interview underneath his video image. This may be done with a special effects generator. A black background is used with white letters. The white letters are centered at the bottom of the screen and the fader control gradually introduces the name of the participant and then fades it from the screen. This technique is referred to as superimposition, ("supers").

Another method developed by the author has been to reverse the video signal making the positive picture a negative. In this way, a blank white file card 5″ x 8″ may be used. The name of the participant is typed on the bottom of the card. The card is placed in the field of a video camera mounted on a titler. Names may easily be typed using a large "orator" type. Using a negative amplifier, the signal may be easily reversed. Instead of a white card, an image of a black card is produced with white type. In this way, the title signal is superimposed on the video image of the participant. A black background superimposed is needed for the black background represents a zero signal or no signal. If used as originally set on a white card with the black typed name, the image of the participant would become all white and no image would be visualized.

There are usually available commercial video inverters and some cameras have such inverters "built-in." In some special effect generators, one of the video inputs may be inverted.

In producing educational video productions, the video inverter may be used to superimpose terminology, to label anatomical parts and roentgen studies.

The cost of such an additional feature may be up to $300 or more.

Recording System

To record images and sound on television, a video tape recorder is used. There are two formats of tape machines that can be used in low budget CCTV systems. There is a half-inch tape recorder and a one-inch video tape recorder. We have a half-inch Craig video tape machine and a one-inch Ampex video tape machine. The cost of the half-inch machine is only three fourths as much as the one-inch machine. The half-inch tape cost is only half as much as the one-inch tape. The Craig machine costing less has many extra features not available on the one-inch Ampex including editing and dubbing of audio sound after the video tape is made, and slow motion. The resolution of the half-inch machine is about equal to that of the one-inch Ampex,

Model 5000. The Veterans Administration has standardized on the one-inch Ampex machine and bi-weekly video tapes are distributed to the Togus V.A. Hospital from the Network for Continuing Medical Education, 15 Columbus Circle, New York.

Conference Room Studio

Our Conference Room has been adapted to be used as a T.V. Viewing System or studio. The two cameras used in radiation therapy may be removed from the wall mounts and placed on wall mounts in the conference room. These two mounts are on both side walls of the conference room and were easily made by our maintenance shop. The viewfinder camera is placed in the center aisle in the back of the room. "The control room" is located in an adjacent room, the private dining room. Wires from all the cameras are run overhead on top of a suspended ceiling. In "the control room" we have three monitors, special effects generator, two final output monitors and a video tape recorder. All the control room equipment has been mounted on two rolling carts. The "VTR," the final output monitor, and audio mixer are mounted on one cart. The other cart contains 3 monitors and special effects generator. A special mounting platform has been designed to place the 3 individual monitors above the special effects generator. Copies of the plan for this platform are available from the author. This platform allows the monitors to be removed and placed in strategic locations during the playback session to a large audience.

A distinct advantage of our remote studio is that it increased the capacity of the conference room from about 80 to 110. The overflow audience may sit in the private dining room and watch the whole program over the closed-circuit television system.

Lights which are very important in television production are suspended from the ceiling. Microphone wires are also run over the suspended ceiling. On the front wall of this conference room, we have a white blackboard. With this white blackboard, water-based markers are used. These show up much better than white chalk. This white blackboard may be used as a projection screen for showing movies, slides and other visuals.

Cine Film for CCTV

Cine x-ray film which is used in routine diagnostic studies can be processed in our department. This film also may be used in a 16mm movie camera. The result of the processed film is a negative and since we do not have printing equipment to produce a positive, this film may be projected as a negative and recorded on television. The video inverter is then used to produce a positive image. The 16mm cine film is projected on a screen and a camera placed very close to the projector recording the image off the screen. Using this procedure, there is a slight but noticeable flicker because the projector projects the film at 24 frames per second while the television records the image at 30 frames per second. Commercial television uses a special projector to eliminate this slight flicker. This projector has a fast pulldown which makes the image remain on the screen for a longer fraction of a second. It has been found that by using a Mylar opaque screen the flicker is reduced. In this case, the image is projected by means of one mirror to the screen. The camera is placed on the other side of the screen to record the image. The flicker is reduced because the Mylar tends to retain the image for a fraction of a second.

Of considerable value in teaching health subjects to the community, is using the prepared video tapes on Cable Television. At least 5 Health Informational Programs have been prepared. Programs may be placed on unused TV Channels by bringing the VTR to the 'Head End' or antenna farm where the signals from commercial TV stations are received and amplified. (The Federal Communications Commission now requires community cable TV to have a TV studio if there are over 3600 subscribers. Our community which has a potential of 6500 will have a 'CATV' Studio by January, 1971).

Conclusion

A description of a basic TV System for use in radiotherapy and continuing medical education for the profession and the community has been presented. The elements of the complete basic system are described including a block diagram. A simple and economical video inverter produced by the author is described and the circuitry presented. If a Craig ½" VTR is available, a health information production will be made available for viewing to demonstrate the use of the system to anyone interested. Copies of plans for the ROC video-inverter, the mobile TV monitor and generator platform, wall mounts, etc., designed by the author will be made available on request.

This work was prepared through an Educational Stipend from the Maine Institute of Continuing Medical Education at the Augusta General Hospital, and was modified from an original more complete work submitted to the Maine Radiological Society in April of 1970.

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Maine Community Medicine and the Maine Institute of Continuing Medical Education

FRANCIS J. O'CONNOR, M.D.*

In the Spring of 1968, the Maine Institute of Continuing Medical Education was established at the Augusta General Hospital with the approval of the Board of Directors to formalize the continuing medical education program.

To call attention to the State and especially the University of Maine the need for a Continuing Medical Education Program, the MICME was evolved and symposia developed as models for the Continuing Education Division of the University of Maine. The University of Maine, because of its widespread campuses in many Maine cities, seemed to be the most logical choice for developing an active Continuing Medical Education program.

Initially the educational institute, because of its proposed broad approach, would be the Maine Institute of Continuing Education (MICE). However, one can easily see the public relations problem which might develop with abbreviated newspaper accounts such as M.I.C.E. at A.G.H.

The following is a listing of the purposes of the MICME evolved during the past 2 years and presented at the FIRST MAINE PROMIS SYMPOSIUM, February 6, 1970, at St. Paul's Center in Augusta.

1. To provide continuing medical education at all levels for physicians, nurses, technologists and all other allied health personnel.
2. To provide through continuing education a quality of health care to all persons of the community. The means to the solution of an increasingly complex problem is through the Problem-Oriented Medical Record[1,2] with the aid of well-trained paramedical assistants in a Problem-Oriented Medical Information Service (PROMIS LAB).
3. To specifically develop and evolve new and economical techniques for the management of clinical problems of cancer, heart disease and stroke, etc., in the Maine Community.
4. To provide a model of Emergency Medical Services and develop an educational plan for an emergency medical service technologist and to make specific attempts to move quality emergency care outside of the hospital to the highways.
5. To stimulate educational programs especially designed for the family physician as the means of restoring and developing the kind of a physician well able to guide the course of problem management with the newest techniques of total patient care.
6. To help "generalize" the specialist as an attempt in promoting more total health care by increasing the number of physicians dedicated to this concept.
7. To recruit physicians to the Maine community.
8. To provide opportunities for medical students and residents to experience the practice of medicine while still in their training perod in the Maine Community, and to aid in the reestablishment of a Medical School in Maine dedicated to Community Medical Practice
9. To relate major medical university centers especially in New England to the Community Hospital and offices of the general practitioners of medicine.
10. To recruit allied health personnel by providing continuing medical education and an opportunity for meaningful responsible employment in health care.
11. To continue to develop community health career programs to stimulate high school students to a career in medicine, and provide early introduction to health careers through a Research Assistant Program in medical technologies.
12. To continue to develop the Augusta Nature Education Center and the Augusta Nature Science Camp to provide youngsters at the grammar school level with the opportunity to learn environmental awareness and natural science as the earliest possible introduction hopefully to a health career.

In future reports, the means to develop and realize the aims and purposes of the M.I.C.M.E. will be described.

It is sincerely hoped that this report may stimulate others in the state charged with medical education and community health care or with the will to improve Community health care to make these same aims and purposes a reality for their own community hospitals.

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DEAN H. FISHER, M.D.
COMMISSIONER

State Of Maine

Department of Health and Welfare

Gonorrhea - A New Look at an Old Problem

CHARLES LINDMAN*

With much of the public's attention being focused on the "new" problems and breakthroughs in the fields of air pollution, water pollution, measles eradication and accident prevention, there is a tendency to forget or ignore the "old" health problems – those that have been around for centuries. One such health problem is gonorrhea. Not only is gonorrhea still present in Maine but it is infecting more people than ever, particularly the young people of this State.

In Maine, gonorrhea is the most prevalent venereal disease of teenagers as illustrated by a 100% increase in the number of reported teenage cases from 1968 to 1969. Over 60% of the infectious syphilis cases reported during 1969 involved teenagers. Overall in the State, there has been a 400% increase in the total number of reported gonorrhea cases from 1962 to 1969. Even with this alarming rise in the number of reported cases, there are many uninformed people who consider gonorrhea no worse than a "common cold." Of course, untreated gonorrhea presents a serious health problem to the infected patient.

Based on the number of reported cases, close to 50% of the 1,000 private physicians in the State are seeing and treating gonococcal infections in their practices. With as significant a disease problem as this, many physicians throughout the State have been confronted with diagnostic and treatment problems. The Division of Communicable Disease Control's medical staff keeps constantly on the alert for new recommendations and techniques in the management of gonorrhea.

Diagnosis and Treatment: The diagnosis of acute gonorrheal urethritis in the male is relatively easy. Laboratory confirmation may be made by smear, using the Gram stain, which is about 99% specific and reliable. To diagnose gonorrhea in women, culture specimens should be obtained from the cervix and inoculated on Thayer-Martin (TM) culture plates. Gram-stained smears are not recommended for the diagnosis of gonorrhea in women. Within the next few months, the State Public Health Laboratory will be testing a new culture transport medium called Trans-grow. This medium will consist of a double strength Thayer-Martin agar placed in 1 oz. rubber capped bottles. When this kit becomes available, it should assist the physician in managing the female patient and at the same time eliminating diagnostic problems.

Physicians in Maine are occasionally confronted with treatment failures but in most instances these treatment problems are caused by inadequate dosage schedules or by the use of oral penicillin which is not the treatment of choice. Presently, the Bureau of Health's recommended treatment schedule still consists of 2.4 million units of aqueous procaine penicillin G for men and 4.8 million units for women in two I M injection sites. Re-treatment may be necessary in 3-4 days if the disease does not respond and if follow-up cultures/smears remain positive.

Of particular importance, during the treatment of the gonorrhea patient, is the possibility of a concurrent case of primary syphilis. Many physicians in the State will take a serologic test for syphilis; however, patients seen in hospital emergency rooms, out-patient clinics, etc. throughout Maine with a gonococcal infection rarely receive a blood test for syphilis. Regarding serology testing, several pilot studies are being conducted in various cities throughout the country to determine the effectiveness of a serological test for gonorrhea; however, clinical application is still a long way off.

Epidemiology: To combat this growing public health menace to the young people of this State, a law passed by the 104th legislative session permits a physician to render medical care to a minor for treatment of venereal disease without first obtaining the consent of a parent or guardian or to inform the parent of such treatment. This law coincides with the AMA endorsement in 1968 which stated that a change in law is needed in those states which do not have existing laws permitting minors to give their own consent for V.D. therapy.

Since the "asymptomatic" reservoir of infection in females is a major contributing factor to the growing problem in this State, a program of screening with routine

*Public Health Advisor, Division of Communicable Disease Control.

cultures on female patients attending family planning clinics around the State has been instituted. Recent figures indicate an almost 3% positive culture return on females who had an unsuspected gonorrheal infection. Those females whose tests are positive receive further evaluation and treatment when indicated. Faced with this increase of "silent" gonorrhea in the female, it is becoming apparent that routine cultures for gonorrhea should be considered in all prenatal, gynecological, family planning and general clinics, as well as the physician's office. This screening practice may dip into the prime reservoir of the disease which is in fact the asymptomatic female carrier.

The Bureau of Health strongly recommends the preventive treatment of female contacts to infected male patients. This service would eliminate from possible infection, the female, who is epidemiologically linked to a gonorrhea case but is clinically negative on smear/culture examination. In Maine, there is little data to adequately evaluate the results of this activity; however, there have been indications that this preventive measure is occurring more frequently.

Epidemiological activities to control the spread of the disease have been somewhat ineffective for the following reasons: the short incubation of the disease which makes it almost impossible to reach exposed persons before the disease has developed; the likelihood that the infected person will seek treatment promptly because of the discomfort it causes (particularly in males); and the sheer size of the gonorrhea problem (100 reported cases per month). During the past year, efforts have been made to reorganize the epidemiological services available to the private physician. When this expertise is requested by a physician, every attempt is made to interview the patient in a confidential situation and then locate all contacts and refer them for immediate examination. Unfortunately, all too frequently, there are few requests made by the physician for this service. When this occurs, the spread of the disease goes unchallenged and consequently the incidence of the disease continues to increase.

In an attempt to establish a closer bridge of communication between the private physician and the Bureau of Health, a new and revised confidential case report will include a central phone number to which a physician may call for direct diagnostic assistance, medical advice of epidemiological services. The new morbidity report form will also contain a section where the physician may list any contact needing immediate follow-up. Many physicians in the State prefer to interview their own patients and then utilize the services of the various health departments for rapid field follow-up. This procedure can terminate the spread of new cases only if the locating information on the contact is accurate and complete.

Information and Education: Of major significance in the battle against gonorrhea has been a resurgence of public awareness programs on V.D., supported by the mass media outlets throughout the State. Television and radio stations around the State have been most cooperative in presenting programs on the subject of venereal disease, particularly gonorrhea. Each time a program has been presented in the State, there are numerous requests for further information on the subject. On several occasions, programs about venereal disease conducted in the urban areas of the State have motivated persons to call the local health departments for assistance on a possible infection.

The goals of our venereal disease education program for the general public are: (a) to bring about behavioral change which would reduce the risk of contracting a venereal disease; (b) to facilitate recognition of venereal disease symptoms and prompt the individual to seek diagnosis and treatment and; (c) to develop attitudes which favor cooperation with the case finding efforts of public health officials.

Informational programs about venereal disease continue to gain acceptance as part of school curriculum around the State. The Bureau of Health's staff has speakers available and an extensive film library on the subject. The objectives of a school venereal disease educational program are to clarify misconceptions which lead to stigmatization of persons who contact a venereal disease and to provide basic information concerning the symptoms and the need for prevention, early diagnosis and treatment. Regardless of how effective any venereal disease education program may be, its maximum effectiveness can only be obtained when it reaches those segments of the State's population where the risk of contracting a venereal disease is high.

The State of Maine, like the rest of the country, is confronted with a gonorrhea problem which at present seems almost impossible to effectively control. Of course, adequate control begins with a cooperative working effort between public and private medicine. Without this joint approach, any new and innovative methodology for the control of gonorrhea will have little affect on the spread of the disease.

Maine Medical Association

STANDING COMMITTEES — 1970-1971

Standing Committees for 1970-1971 as proposed by the Nominating Committee and approved at the Second Meeting of the House of Delegates of the Maine Medical Association at Kennebunkport, Maine, June 7, 1970.

Nominating Committee

1st District – DAVID K. LOVELY, M.D., Portland
2nd District – JOHN R. FENGER, M.D., Norway
3rd District – GEORGE W. BOSTWICK, M.D., Newcastle – *Chairman*
4th District – GEORGE L. TEMPLE, M.D., Belfast
5th District – KARL V. LARSON, M.D., East Machias
6th District – CHARLES H. LIGHTBODY, M.D., Guilford

Scientific Committee

L. Armand Guite, Jr., M.D., 45 Elm St., Waterville (1 yr.) – Chairman
Bradley E. Brownlow, M.D., Blue Hill Mem. Hospital, Blue Hill (2 yrs.)
Robert H. Pawle, M.D., 251 U. S. Rt. 1, Falmouth (3 yrs.)

Legislative Committee

Lloyd G. Davies, M.D., 249 Ocean House Rd., Cape Elizabeth (2 yrs.) – Chairman
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James H. Bonney, M.D., 53 Chadwick St., Portland (1 yr.)
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John Kazutow, M.D., Box 113, Columbia Falls (1 yr.) – (Washington)
Andre P. Fortier, M.D., 68 Foss St., Biddeford (3 yrs.) – (York)

Continue on Page 174

PROTEIN CONTENT / 7 oz. Serving*

Bean with Bacon	6.8	Green Pea with Ham (Frozen)	7.6
Beef	8.0	Hot Dog Bean	8.4
Chicken Broth	5.5	Pepper Pot	6.1
Chicken 'N Dumplings	5.8	Split Pea with Ham	10.2
Chili Beef	6.2	Vegetable Beef	5.0
Green Pea	6.9	Vegetable with Beef (Frozen)	5.4

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(when her husband's at fault)

Flagyl® brand of metronidazole

Cures Trichomoniasis in Both Women and Men

About half of all husbands of infected women harbor *Trichomonas vaginalis*.*

Few of these men have symptoms. Even so, all are capable of perpetuating the infection and rendering treatment of a woman alone futile.

Only a systemically active medication like Flagyl is capable of reaching the hidden reservoirs of infection in the genitourinary tracts of both men and women.

Only Flagyl has been able to achieve rates of cure consistently above 90 per cent and often up to 100 per cent in trichomonal infections in both men and women.

Indications: For the treatment of trichomoniasis in both male and female patients and the sexual partners of patients with a recurrence of the infection provided trichomonads have been demonstrated by wet smear or culture.

Contraindications: Evidence of or a history of blood dyscrasia, active organic disease of the central nervous system and the first trimester of pregnancy.

Warnings: Use with discretion during the second and third trimesters of pregnancy and restrict to patients not cured by topical measures. Flagyl (metronidazole) is secreted in the breast milk of nursing mothers. It is not known whether this can be injurious to the newborn.

Precautions: Mild leukopenia has been reported during Flagyl use; total and differential leukocyte counts are recommended before and after treatment with the drug, especially if a second course is necessary. Avoid alcoholic beverages during Flagyl therapy because abdominal cramps, vomiting and flushing may occur. Discontinue Flagyl promptly if abnormal neurologic signs occur. There is no accepted proof that Flagyl is effective against other organisms and it should not be used in the treatment of other conditions. Exacerbation of moniliasis may occur.

Adverse Reactions: Nausea, headache, anorexia, vomiting, diarrhea, epigastric distress, abdominal cramping, constipation, a metallic, sharp and unpleasant taste, furry or sore tongue, glossitis and stomatitis possibly associated with a sudden overgrowth of *Monilia*, exacerbation of vaginal moniliasis, an occasional reversible moderate leukopenia, dizziness, vertigo, drowsiness, incoordination and ataxia, numbness or paresthesia of an extremity, fleeting joint pains, confusion, irritability, depression, insomnia, mild erythematous eruptions, "weakness," urticaria, flushing, dryness of the mouth, vagina or vulva, vaginal burning, pruritus, dysuria, cystitis, a sense of pelvic pressure, dyspareunia, fever, polyuria, incontinence, decrease of libido, nasal congestion, proctitis, pyuria and darkened urine have occurred in patients receiving the drug. Patients receiving Flagyl may experience abdominal distress, nausea, vomiting or headache if alcoholic beverages are consumed. The taste of alcoholic beverages may also be modified.

Dosage and Administration: *In the Female.* One 250-mg. tablet orally three times daily for ten days. Courses may be repeated if required in especially stubborn cases; in such patients an interval of four to six weeks between courses and total and differential leukocyte counts before, during and after treatment are recommended. Vaginal inserts of 500 mg. are available for use, particularly in stubborn cases. *When the vaginal inserts are used* one 500-mg. insert is placed high in the vaginal vault each day for ten days and the oral dosage is reduced to two 250-mg. tablets daily during the ten-day course of treatment. Do not use the vaginal inserts as the sole form of therapy. *In the Male.* Prescribe Flagyl only when trichomonads are demonstrated in the urogenital tract, one 250-mg. tablet two times daily for ten days. Flagyl should be taken by both partners over the same ten-day period when it is prescribed for the male in conjunction with the treatment of his female partner.

Dosage Forms: Oral tablets . . . 250 mg.
Vaginal inserts . . 500 mg.

*References available on request.

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Research in the Service of Medicine

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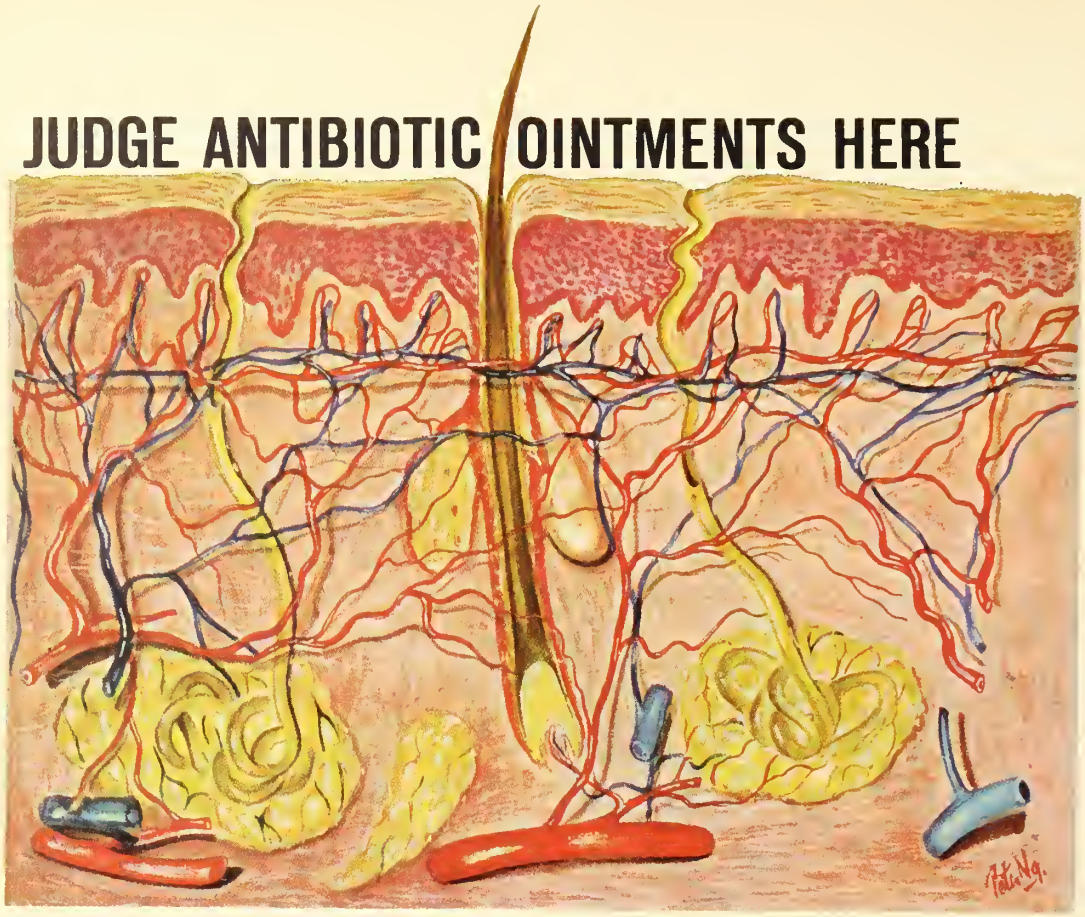

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Caution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

Supplied: Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.

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The Journal of the Maine Medical Association

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Across The Desk

Standardized Medical History and Exam Forms Endorsed by Maine State Principals' Association

"The Maine State Principals' Association has endorsed and decided to start using this fall the standardized medical history and exam forms designed by the Maine Medical Association's Special Committee on the Medical Aspects of Sports. These forms, plus a "Parental Consent" form, were presented in an article in the Nov. 1969 issue of our Journal by Dr. Russell Lane, Committee Chairman and Athletic Team Physician at the University of Maine in Orono. The forms have been printed and distributed to Maine High Schools through the SPA central office. The Committee would like to urge all physicians to give the medical evaluation of our prospective high school athletes, including the forms on which the evaluation is recorded, their sincerest consideration, so that we can be said to be positively contributing to the health and fitness of this segment of our youth." – Ed.

Briefly in the News:

COST OF MEDICAL CARE is rising so fast in England, new ways may be needed to finance it. During visit to UCLA medical school, *Lord Brock,* noted British surgeon, said when costs become greater than gov't. may be willing to accept, there are only 2 alternatives: reduce services or find new way of financing existing level of care. One solution, opposed by most politicians and patients, is to have patient pay part of cost.

"*Two years ago* I would have said nat'l. health insurance is inevitable in U.S., but I must now modify my view," Lord Brock said. "More people in this country are realizing what British already have learned – that costs are much greater than anticipated."

COMPUTERS MAY BE the manpower and cost-control answer for health care industry. And experts see full scale computerized revolution in health care procedures during this decade.

To ease manpower shortages, computers will take over critical patient care and surgical monitoring. Electrocardiograms, respiratory curves and blood pressure curves already are machine processed. Some centers also process medical histories and lab tests.

Patients now hospitalized for routine diagnostic tests will be handled as outpatients in automated diagnostic process, freeing hospital beds for emergency cases.

If average length of a hospital stay were reduced by only a day Americans would save $1.7 billion a year, says *Health Insurance Institute.*

Most hospitals now use computers mainly for billing, ordering and payroll. But as computer vendors begin producing special purpose units to process medical signals at moderate costs, hospitals, clinics and nursing homes will tie into automated medical systems. There are 700 computers in hospitals now.

If computers could increase efficiency of all U.S. MDs by just 4%, it would be equivalent to doubling graduating classes of all U.S. medical schools.

DESPITE FACT 49 states now allow MDs to incorporate, there has been no great rush among physicians to form corporations. Some object to complex, expensive corporate rituals they must observe. To make incorporating worthwhile, MD should make at least $35,000 and be able to put aside $5,000 to $10,000 annually toward retirement.

Federal gov't. has amended its regulations governing care in *Intermediate Care Facilities* to give states greater flexibility in determining standards for care beyond those specified in *Social Security Act.* ICF are residential accommodations offering more than room and board but less care than skilled nursing homes. New amendments appeared in *Federal Register* June 10. – *Medical News Report, Vol. 2, Number 24, June* 15, 1970.

Continued on Page 173

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Electrocardiographic Left Ventricular Hypertrophy and Risk of Coronary Heart Disease

The natural history of coronary heart disease, . . . is best discerned from an epidemiologic investigation of the way it evolves in a general population. . . . at Framingham, Mass., where 5,127 men and women have been followed for the development of initial attacks of coronary heart disease, electrocardiograms have been obtained biennially on 7 successive examinations over a 12-year period. Previous study . . . had shown an electrocardiographic pattern of left ventricular hypertrophy to be a strong predictor of clinical coronary heart disease.

A wide variety of ECG abnormalities are reported to occur commonly in persons with clinically overt coronary heart disease.

Aside from the pathognomonic diagnostic ECG findings of myocardial infarction, the other ECG findings may be coincidental, may be nonspecific manifestations of myocardial pathology regardless of cause, the result of therapy for cardiovascular impairments, or a cardiac manifestation of hypertension. The ECG pattern of LVH is commonly found in association with coronary heart disease. It has been noted clinically, and now epidemiologically, to frequently precede symptomatic coronary heart disease.

. . . Since an ECG pattern of "definite" LVH, including S-T and T wave abnormality, is associated with a striking increase in risk of symptomatic coronary heart disease and this is true even after adjusting for associated hypertension, it is tempting to hypothesize that this too is an occult manifestation of coronary heart disease. . . . The "possible" ECG-LVH pattern associated largely with increased QRS voltage (without significant S-T and T abnormalities) may well reflect only the associated hypertension that predisposes both to anatomical hypertrophy of the left ventricle and to coronary heart disease, since the excess risk of coronary heart disease associated with this pattern is obliterated when adjustment is made for hypertension.

. . . impaired coronary blood flow makes a contribution to the ECG pattern of LVH and is compatible with the epidemiologic findings herein reported. The dominant cause of left ventricular hypertrophy, . . . is hypertension. Anatomical hypertrophy of the left ventricle associated with hypertension seldom occurs in the absence of a significant degree of coronary atherosclerosis. It is reasonable to assume that this is also the case with regard to ECG-LVH in hypertensives. . . .

. . . persons predisposed to coronary heart disease by atherogenic factors . . . who develop a "definite" pattern of ECG-LVH deserve management equivalent to that offered those with established overt coronary heart disease. This is justified by the strong possibility that the appearance of this ECG abnormality without other explanation . . . may well be a hallmark of the onset of ischemic myocardial involvement as a result of a compromised coronary circulation. Because the initial presenting complaint . . . is all too often also the very last, a broadening of the clinical spectrum to include the asymptomatic phase of the disease is imperative. There is good evidence that this may be achieved by periodic ECG examination for changes of silent myocardial infarction and LVH at rest. . . . the postexercise ECG provides a means for the still earlier detection of a physiologically significant degree of impairment of coronary circulatory capacity. . . .

The appearance of a pattern of ECG-LVH must be regarded as a grave prognostic sign carrying a high risk of clinically overt coronary heart disease and of premature death. . . . this ECG abnormality is at the very least a potent factor of risk in coronary heart disease if not an early asymptomatic manifestation of the disease. . . . Such highly vulnerable persons merit vigorous prophylactic efforts aimed at delaying the onset of symptomatic, lethal coronary heart disease.

Submitted by Jacob B. Dana, M.D., Maine Heart Association

Reference — Kannel, William B. et al, Annals of Internal Medicine, Volume 72, Pages 813-822, 1970

President

Maine Medical Association

1970-1971

CHARLES R. GLASSMIRE, M.D.

Charles Robert Glassmire, M.D. of South Portland, Maine became the 121st President of the Maine Medical Association at the 117th Annual Session banquet on June 8, 1970. Dr. Glassmire served as Councilor for the First District from 1966 to 1969; the last year as Council Chairman, and as President-elect from 1969 to 1970.

Dr. Glassmire was born in Brooklyn, New York on May 15, 1920, son of Dr. Charles M. and Gretchen R. Glassmire. He was graduated from the Mercersburg Academy in 1937, received his A.B. in 1941 and his M.D. in 1944 from the University of Pennsylvania. He interned and served a residency at the Maine General Hospital in Portland, Maine, and later a fellowship in Rheumatology at the New England Center Hospital in Boston, Massachusetts. He served for two years as a Medical Corps Officer in Germany with the United States Army.

Dr. Glassmire is a member of the American Medical Association, the Maine Medical Association, the Cumberland County Medical Society, the New England Rheumatism Association, the American Rheumatism Association, the Maine Society of Internal Medicine and the American Society of Internal Medicine. He has been an attending physician on the Medical Service of the Maine Medical Center since 1946, and on the staff of the Mercy Hospital in Portland.

Dr. Glassmire is active in many community affairs, but most of his time away from medicine is spent in Masonry. He is active in all branches and at present is Deputy Grand Master of the Most Worshipful Grand Lodge of Maine.

Dr. Glassmire is married to the former Ruth Elizabeth Dearborn of Oak Park, Illinois. They have one son, Charles R. Glassmire, Jr., and two daughters, Mrs. Edward R. Hanson and Beth. They have one grandson.

Elected at the 117th Annual Session of the Maine Medical Association

Kennebunkport, Maine June 7, 8, 9, 1970

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DR. WOOD

PATRICIA A. BERGERON

MRS. BERGERON

It's not an easy task to take over the tiller when the sloop is on a new course, and the same old crew is manning the lines — but Patti is up to the task.

In its 110 years, the Maine Medical Association and its Journal has had only 4 Secretary-Treasurers. The 5th, Patricia A. Bergeron, was elected by the Council on Sunday, June 7, 1970.

Employed by the Maine Medical Association since 1962, she has continuously advanced her knowledge of the Association and its operations. Like Esther — she has done more than "the duty requires"; her ability and pleasant cooperative personality, her willingness to work, and the help she will receive from all the membership — should make Patti's task a rewarding, — and we all hope, a long one.

E. M. K.

At the 117th Annual Session of the Maine Medical Association, change was the order of the day. A new location — The Colony at Kennebunkport — a new and different format for the scientific program, and the House of Delegates set up the mechanism for sweeping changes in direction for the Maine Medical Association.

There was however, one big change that was tinged with more than a little bit of sadness — Esther retired as Secretary-Treasurer of the M.M.A. after 42 years of dedicated service to the Association. This event, well marked by Dr. Branch's presentation and Esther's election to Honorary Membership, released a flood of memories for us all.

"Change" is not a new experience for Esther —

From the back room of Dr. Gilbert's office, she literally moved the Maine Medical Association to the Maine General Hospital; to 142 High Street, Portland, and then to the Bowdoin Campus, a saga which we all hope she will record in the leisure hours of her retirement.

If the acclaim at the meeting had been for an honorary degree instead of Honorary Membership, the citation would have read —

- Good and faithful servant
- Business Manager and shepherd for 40 volumes of The Journal
- Friend, Advisor and Chief Organizer for 36 Presidents
- Keeper of the Books — Through good times and bad
- Recorder of our words and actions (only the good ones)
- Storehouse of factual data
- Recaller of names and dates, and places and policies, disremembered by us all
- Steady, patient guide and listener

You have done your work well and earned our love and respect. Enjoy your leisure, but save some time to help us through yet another change.

IN ADDITION TO HER OTHER DUTIES!

AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

T.V. Series "Why You Smoke" Helps Cigarette Smokers to Quit

ATLANTA, GA. — One out of 20 persons who watched the nationwide TV series on "Why You Smoke" quit smoking cigarettes following the programs, according to an American Cancer Society study.

These preliminary results were made known at the American Cancer Society's national Public Information Committee meeting at the Marriott Motor Hotel. The findings were based on a study made in 11 metropolitan areas including Atlanta. The Committee met in conjunction with the ACS National Board of Directors.

The five percent decline in smoking occurred among viewers who saw at least one of five programs broadcast by the National Educational Television (NET) network in March.

"The study, when completed, can provide guidelines for helping cigarette smokers to quit," William B. Lewis, ACS Board Chairman said. He said the NET listening audience was a large one and called the series a highly successful experiment. "Even at this point in the findings," he said, "it appears that television can be remarkably effective in helping cigarette smokers kick their habit."

The series included audience participation through a smoker's self-test to help individuals understand why they smoked, how much they knew about their habit and how much they wanted to change it. The series was produced under a grant from the American Cancer Society which has been conducting a nationwide program of education on the health perils of cigarette smoking.

The programs focused on the experience of several families and individuals in Washington, D.C., whose "case histories" were followed during the five broadcasts. The subjects faced up to the facts of their smoking habits and attempted to change them. Some were successful while others were unable to overcome their attachment to cigarette smoking.

The study, conducted for the ACS by Lieberman Research, Inc., of New York, principally attempted to measure the effects of the TV programs on smokers and included a group of 7,177 men and women. They were contacted by telephone in the 11 cities — Atlanta, Boston, Chicago, Cincinnati, Cleveland, Pittsburgh, Rochester, N.Y., San Francisco, Seattle, Tampa and Wilmington, Del.

About 12 percent of those questioned had seen at least one of the programs and by comparing the smoking habits of this group with an equal number of persons who did not see the series, conclusions could be drawn as to the impact of the series.

Five percent of those who saw one or more programs had quit smoking whereas there had been no new abstainers among the control group. Other changes in smoking habits were effected by the TV series. The more than one-pack-a-day smokers among the viewers declined from 30 to 24 percent while the non-viewers remained essentially the same, declining from 31 to 30 percent.

The average number of cigarettes smoked daily among viewers declined from 18.1 to 15.1, a decrease of nearly 17 percent while among non-viewers a smaller decline took place. The average number of cigarettes smoked daily for non-viewers for the same period dropped 1.4, a decline of about 6 percent.

These initial results were announced from the analysis made several weeks after the telecasts. A follow-up of those who have quit smoking along with a group of controls for comparison also is under way, it was announced by the American Cancer Society whose volunteers conducted the telephone surveys.

A final follow-up will be made in the fall to obtain long-term results, particularly to determine if those who quit smoking have been able to stay away from cigarettes.

American Cancer Society News Service Release

The girth control pill

Tepanil® Ten-tab
(continuous release form)

(diethylpropion hydrochloride)

works on the appetite not on the 'nerves'

When girth gets out of control, TEPANIL can provide sound support for the weight control program you recommend. TEPANIL reduces the appetite—patients enjoy food but eat less. Weight loss is significant—gradual—yet there is a relatively low incidence of CNS stimulation.

Contraindications: Concurrently with MAO inhibitors, in patients hypersensitive to this drug; in emotionally unstable patients susceptible to drug abuse.

Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported. Sympathomimetic cardiovascular effects reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others. *Allergic phenomena* reported include such conditions as rash, urticaria, ecchymosis, and erythema. *Gastrointestinal effects* such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tablet daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet three times daily, one hour before meals. If desired, an additional tablet may be given in midevening to overcome night hunger. Use in children under 12 years of age is not recommended.

T-006A / 1/70 / U.S. PATENT NO. 3,001,910

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DIVISION OF RICHARDSON-MERRELL INC.
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Painful night leg cramps...

unwelcome bedfellow for any patient—including those with arthritis, diabetes or PVD

One thing patients can sleep without, particularly patients with chronic disease conditions such as arthritis, diabetes or PVD, is painful night leg cramps. Although seldom the presenting complaint, night leg cramps can tie your patients up in painful knots. Now, just one tablet of QUINAMM at bedtime can usually bring an end to shattered sleep and needless suffering. Your patients will sleep restfully—gratefully—with QUINAMM, specific therapy to prevent painful night leg cramps.

Prescribing Information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions/Adverse Reactions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

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Quinamm™ Specific therapy for night leg cramps
(quinine sulfate 260 mg., aminophylline 195 mg.)

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CONFERENCE ON PREMATURE AND HIGH-RISK NEWBORN INFANTS

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Wednesday, September 2, 1970

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Division of Maternal & Child Health, State of Maine
Department of Health & Welfare

PROGRAM

9:30 A.M. Introduction – Maurice Ross, M.D., Chairman; Maine Chapter, American Academy of Pediatrics, Program Chairman

9:35 A.M. The Obstetrician's Role – Howard N. Jacobson, M.D., Director, Macy Program, Boston Hospital for Women, Lying-In Division

10:30 A.M. The Anesthesiologist's Role – John E. Mazuzan, M.D., Associate Professor of Surgery (Anesthesia), University of Vermont

11:25 A.M. The Pediatrician's Role – Joseph L. Kennedy, M.D., Director of Nurseries, St. Margaret's Hospital, Assistant Professor of Pediatrics, Tufts University School of Medicine

12:30 P.M. Luncheon – Shawmut Inn Dining Room

1:45 P.M. Workshop Discussions (Bring problems for discussion)
Obstetrics – Robert M. Knowles, M.D., Portland
Howard N. Jacobson, M.D.
Anesthesiology – Chester W. White, Jr., M.D., Maine Medical Center
John E. Mazuzan, M.D.
Pediatrics – John C. Serrage, M.D., Portland
Joseph L. Kennedy, M.D.

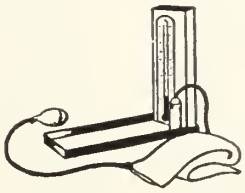
3:00-3:30 P.M. Recess

3:30 P.M. Summation by Drs. Knowles, White, and Serrage, followed by Panel Discussion including all speakers

5:00 P.M. Social Hour – Cocktails

6:00 P.M. Dinner in Shawmut Inn Dining Room, followed by meetings of individual societies

NOTE: A Pre-registration form for the Conference was mailed to the members of the Maine Medical Association in July.



County Society Note

WASHINGTON

A regular meeting of the Washington County Medical Society was held on June 29, 1970 at the Peabody Memorial Library in Eastport, Maine with ten members and guests present. George B. Shaw, M.D., President of the Washington County Medical Society, presided. He introduced Randall H. Silver, M.D., President of the Hancock County Medical Society, who discussed the Maternal and Infant Care Program. Dr. Silver said that Drs. Brownlow, Stewart and Van Pelt from Hancock County met with Dean Fisher, M.D. of the State Department of Health on June 4th. The relative results of this meeting were that it seems very probable that the MIC program will be reinstituted. Dr. Fisher suggested that the Washington and Hancock County Societies meet together to provide some joint resolution of intent, so that the project could be started again. Dr. Silver also presented some new directions for the MIC project for discussion. This proposal was outlined by John B. Truslow, M.D. Dr. Silver also read a letter from Margaret Dunham, M.D. of the Department of Health and Welfare, Augusta, Maine that was sent to Morris A. Lambdin, M.D. of Ellsworth, Maine in regard to the MIC program. Certain aspects of this program will be continued at least until September. Dr. Silver was asked to take the following resolution to Dr. Dean Fisher, that:

"The Washington County Medical Society goes on record as supporting the concepts of improving medical and social care embodied in the MIC program and urges the development of a new program embodying these concepts that would be acceptable to the medical profession in this area."

James C. Bates, M.D., Councilor of the Fifth District and Donald M. Robertson, M.D., Delegate to the Maine Medical Association, reported on the June meeting of the Maine Medical Association. Dr. Robertson reported that the Society voted in favor of most of the subcommittee reports, except for the re-districting report. They felt that this should be further studied and a committee was appointed to further study this report. Robert G. MacBride, M.D. has been appointed to that committee.

Dr. MacBride read a letter of recommendations about election of Councilors by the nominating committee. The nominating committee is to present the names of two candidates for each position to be filled on the council – also for the President and President-elect – and the council members will be elected from the floor at one of the meetings. There will be three meetings of the House of Delegates during the year. No more than two council members can be from any one district and there will be seven members of the council. It was suggested by John Kazutow, M.D. that the members be increased to ten, so that we would not lose our representation. Dr. MacBride stated that he would bring this up for a discussion at the committee meeting.

There was some discussion by Dr. Silver and Dr. Robertson of the formation of a Foundation for Medical Care. Bradley E. Brownlow, M.D. brought this up at the M.M.A. meeting following his visit to the West Coast. A somewhat similar organization apparently is to be set up in the Rockland and Camden area, known as the Penobscot Bay Medical Center. Dr. Shaw appointed Dr. Robertson as a convener of a committee to look into establishing a similar Foundation in this locality.

KARL V. LARSON, M.D., *Secretary*

News, Notes and Announcements

Subjects Announced for 1970 Essay Contest

The Trustees of the Caleb Fiske Fund of the Rhode Island Medical Society, the oldest medical prize essay competition in America, announce two subjects for the 1970 essay contest:

"The Crisis with Hallucinogenic Drugs – Possible Solutions"

and

"Human Cell Cultures in the Diagnosis of Disease"

A cash prize of $500 is offered for the best dissertation on either subject. Essays must be submitted by December 15, 1970, and must be typewritten, double-spaced, and not in excess of 10,000 words.

For additional information write to the Secretary, Caleb Fiske Fund. Rhode Island Medical Society, 106 Francis Street, Providence, Rhode Island 02903.

Military Surgeons to Hold 77th Annual Meeting

Emphasizing the theme "Controversies in Medicine," medical officers of the three military services will convene with physicians of the Public Health Service and the Veterans Administration for the 77th Annual Meeting of the Association of Military Surgeons of the United States, to be held at the Washington Hilton Hotel on 29 November through 2 December, VADM George M. Davis, MC, USN, the Surgeon General of the Navy and President of the Association, has announced.

Medicine's top man in the Nixon Administration, Dr. Roger O. Egeberg, the Assistant Secretary for Health, Education and Welfare, will deliver the keynote address on Monday morning, 30 November.

As currently planned, the Scientific Program, under the direction of RADM George H. Reifenstein, MC, USNR, will begin with a discussion on "Controversies of Management: Inflammatory Bowel Disease," with W. M. Lukash, MC, USN as Chairman, assisted by LTC W. Boyce, MC, USA as Co-Chairman.

Other topics of clinical medical interest will include panel discussions centering on "Controversies in Management of Neurosurgical Problems, Intercranial Foreign Bodies . . .," moderated by C. Hunter Shelden, M.D., and "The Federal Physician's Attitude Toward Alcoholism," moderated by CAPT C. L. Waite, MC, USN. CAPT Waite's panel will also discuss "Computers and Medicine, a Perspective." These panels will be conducted on Tuesday, 1 December, and Wednesday, 2 December, respectively.

Following the Awards Program on Tuesday, an additional panel will take as its topic, "Problems Involved in Integrating Teaching and Research." The program will be chaired by CAPT J. William Cox, MC, USN.

COL Nelson Irey, MC, USA Ret. will deliver the Sustaining Membership Lecture entitled, "Controversies of Diagnosis: Alleged Drug Reactions." RADM F. P. Ballenger, MC, USN, the General Chairman of the convention, will act as moderator.

The William C. Porter Lecture in Psychiatry will be given this year by CAPT Ransom Arthur, MC, USN. His paper is entitled, "Success is Predictable." The Porter Lecture was es-

tablished in 1958 by the Association, which has been called the Medical Society of the Federal Agencies, to honor William C. Porter, a pioneer in military psychiatry.

Concluding the Scientific Program will be a discussion on "Management of Maxillofacial Trauma." Giving the oral surgical viewpoint will be CAPT Ernest W. Small, DC, USN. CDR Hugh O. DeFries, MC, USN will discuss the medical viewpoint.

In addition, Sections Programs will be held in Health Care Administration, Medical Specialties and Bio-medical Sciences, Dentistry, Nursing, Pharmacy, and Veterinary Medicine, all following the same general theme of "Controversies in Medicine."

Military Patients Treated at Civilian Facilities

The United States Army Hospital, Fort Devens, has assumed administrative authority to process all physician claims for active army personnel treated in a civilian hospital and to provide transportation to the hospital from a civilian facility when medically feasible.

To facilitate the payment of claims, physicians requesting such payment should include on their invoices the following information:

1. Prepare in quadruplicate an itemized statement for each patient for all services and charges giving the patient's full name, rank, and social security number and his organization.
2. Provide a complete diagnosis of the patient's illness or injury; if an injury include how it happened (i.e. auto accident), when (i.e. date and time) and at what location (i.e. intersection of Rtes. 128 and 30).
3. Type and sign the certification which follows:

"I certify that the above charges are true and correct; that services were rendered and necessary in the proper care of the patient; that charges do not exceed prevailing rates for this vicinity; and that payment has not been received."

Name and title

To expedite the transfer of active army personnel to the Fort Devens Hospital, please call the Registrar's Office and give the specific details.

World Health Organization Fellowships Available to United States Health Workers

The World Health Organization will make available in 1971 to United States citizens engaged in operational or educational aspects of public health, a limited number of short-term fellowships for travel abroad related to the "improvement and expansion of health services" in the United States.

In selecting applications a special committee will consider the professional background of the individual, the field and locale of the study proposed, and the utilization of the experience by the applicant on his return. Employees of the Federal Government are not eligible. Applications will not be considered for the prosecution of pure research projects, for attendance at international meetings, nor from students in the midst of training at either the undergraduate or graduate level.

A fellowship award will cover per diem and transportation. Except in very unusual circumstances, it will be limited to short-term travel programs, i.e., two to four months. Employers of successful applicants will be expected to endorse applications and to continue salary during the fellowship.

Priorities of award will be established up to the total of the funds available. The deadline for the receipt of applications is September 30, 1970.

Further information and application forms may be obtained from Dr. Robert W. Jones, III, Chief, Foreign Students Education Branch, Bureau of Health Professions Education and Manpower Training, National Institutes of Health, Public Health Service, Room 1014, HEW-S, Washington, D.C. 20201.

ACROSS THE DESK

Continued from Page 165

American Hospital Assn. favors combining Parts A & B of Medicare program rather than establishing proposed Part C. In testimony before *Senate Finance Cmte.*, AHA recommended combined A & B be financed thru payroll tax. . . . Chicago's *Cook County Hospital* was given autonomy by Illinois Legislature and may contract with Chicago medical schools to provide services and personnel. . . . For free copy of *Smith Kline & French Labs Services Catalog '70/'71,* listing films, booklets, periodicals and services available to MDs, write: Services Dept., E-10, SK&F, 1500 Spring Garden St., Philadelphia, 19101. . . . U.S. District judge dismissed suit filed by 8 Kentucky tobacco growers who attempted to stop 3 major TV networks from broadcasting anti-smoking messages. . . . *Joel Kaplan,* MD, former Army doctor in Vietnam, said 50 to 80% of American troops in Indochina have tried marijuana and other drugs and 10 to 20% could be described as addicts. . . . Recent survey showed hospitals in NY City need 8,791 full-time MDs, dentists and other health personnel. Largest unmet needs are in nursing services with shortage of 2,891 RNs, 700 licensed practical nurses, 1,545 nursing aides and orderlies. – *Medical News Report, Vol.* 2, *Number* 23, *June* 8, 1970.

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Contraindication: Hypercalcemia; neoplastic diseases; and fully digitalized patients. Do not use intramuscularly in infants and young children. Before starting therapy, consult complete product literature.

Write for free copy of "Calcium: The Ubiquitous and Essential Element" and for samples.

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STANDING COMMITTEES – 1970-1971

Continued from Page 164

Members of the Advisory Committee to the Health Insurance Committee

Maine Society of Anesthesiology – Clement S. Dwyer, M.D., 83 Essex St., Bangor

Maine Chapter, American Academy of General Practice – John D. Denison, M.D., 89 Hospital St., Augusta

Maine Society of Obstetrics and Gynecology – E. Allan McLean, M.D., 29 Deering St., Portland

Maine Chapter, American Academy of Pediatrics – Everett A. Orbeton, M.D., 131 Chadwick St., Portland

Maine Society of Internal Medicine (Includes Medical Specialty Group) – Albert Aranson, M.D., Maine Medical Ctr., Portland

Section on Ophthalmology of the M.M.A. – Jay K. Osler, M.D., 74 Birch St., Bangor

Maine Radiological Society – John F. Gibbons, M.D., 22 Bramhall St., Portland

Maine Chapter, American College of Surgeons – John F. Reynolds, M.D., 325 Kennedy Dr., Waterville

Ear, Nose and Throat Group – Loring W. Pratt, M.D., 325 Kennedy Dr., Waterville

Maine Society of Pathologists – Franklin F. Ferguson, M.D., 22 Bramhall St., Portland

Neurology and Neurosurgery Group – Daniel A. Rock, M.D., 477 Main St., Lewiston

Maine Trauma Committee – H. Carl Amrein, M.D., 29 Weston Ave., Madison

Veterans Affairs Committee – Harry B. Eisberg, M.D., 357 Elm St., Biddeford

Maine Psychiatric Association – Reuben Leitman, M.D., 188 Sabattus St., Lewiston

Maine Academy of Orthopedic Surgeons – Philip L. Archambault, M.D., 346 Main St., Lewiston

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Delegate and Alternate Delegate to AMA

(January 1, 1969 to January 1, 1971)
(January 1, 1971 to January 1, 1973)

Delegate – George W. Wood, III, M.D., 156 No. Main St., Brewer

Alternate Delegate – Richard P. Laney, M.D., 50 Water St., Skowhegan

CORRECTION

Honorary Pin Recipients. – In the write-up on Thomas A. Devan, M.D. under Sixty-Year Pin, Penobscot County, published in the June issue, page 128, two errors occurred.

The line "He was House Physician at the Peter Bent Brigham Hospital . . . " should have read, "He was Assistant Director at the Peter Bent Brigham Hospital . . . ."

The line ". . . Director of the Massachusetts General Hospital . . ." should have read ". . . Assistant Director of the Massachusetts General Hospital. . . ."

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*An estimated 208,000 patients have received GARAMYCIN Injectable to date. The combined population of Bangor, Lewiston, and Portland is 144,500. (Estimated 1969 figures from The New York Times Encyclopedic Almanac 1970.)

See Clinical Considerations section on last page...

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Patients with Normal Renal Function

Total Daily Dose (administered in two, three, or four divided doses)			
	Less Severe	Resistant/ Moderately Severe	Serious/Life-Threatening
Urinary Tract Infections (due to susceptible strains of gram-negative bacteria)†	0.8-1.2 mg./kg. for 7-10 days	Larger doses or additional antibacterial therapy should be considered in severe urinary tract infections or in resistant cases involving the renal parenchyma or anatomic anomaly.	up to 5 mg./kg.
Other Infections including bacteremia, infected surgical wounds, severe soft tissue infections, and respiratory tract infections (due to susceptible strains of gram-negative bacteria)	3 mg./kg. for 7-10 days		

†Alkalinization of the urine may be a useful therapeutic adjunct.

Patients with Impaired Renal Function

To minimize the risk of ototoxicity in patients with impaired kidney function, only the first dose should be that normally recommended. Each subsequent dose should be half or less of that recommended for patients with normal renal function, depending upon the degree of renal impairment.

In patients with renal failure who are undergoing 14-hour hemodialysis twice weekly, administration of 1 mg./kg. GARAMYCIN Injectable at the end of each dialysis period has been suggested.

Clinical Considerations

Indications: GARAMYCIN Injectable is clinically effective in infections due to susceptible strains of gram-negative bacteria, including *Pseudomonas aeruginosa*, and species of indole-positive and indole-negative *Proteus*, *Escherichia coli*, and *Klebsiella-Aerobacter*. Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose. If the susceptibility tests indicate that the causative organism is resistant to gentamicin sulfate, other appropriate antibiotic therapy should be instituted.

IN VITRO INHIBITION OF CLINICALLY IMPORTANT BACTERIA BY GENTAMICIN SULFATE (TUBE DILUTION STUDIES)

BACTERIA	No. of Strains Tested	No. of Strains (%) Inhibited by: 4 mcg./cc. or less		8 mcg./cc. or less*		No. of *In Vitro* Studies
Staphylococcus aureus	1,210	1,200	(99%)	1,206	(99%)	11
Pseudomonas aeruginosa	885	771	(87%)	828	(93%)	16
Escherichia coli	836	736	(88%)	779	(93%)	11
Indole-positive and indole-negative *Proteus* species	477	210	(44%)	358	(75%)	12
Klebsiella-Aerobacter species	292	205	(70%)	231	(79%)	10

*Number of strains (%) of gram-negative bacteria inhibited by 10 mcg./cc. or less are as follows: *Pseudomonas aeruginosa*, 828 (93%); *Escherichia coli*, 792 (95%); *Proteus* species, 393 (82%); *Klebsiella-Aerobacter* species, 284 (97%). From same studies as above.
Source: Package Insert

This drug should be limited to the treatment of serious infections caused by gram-negative bacteria, particularly *Pseudomonas aeruginosa*, *Proteus* and other susceptible organisms, with due regard for relative antibiotic toxicity. Therefore, the drug should be considered for use against gram-negative: 1. Bacteremia; 2. Infected surgical wounds; 3. Severe soft tissue infections, including burns complicated by sepsis; 4. Respiratory tract infections; and 5. Selected cases of urinary tract infection.

Contraindications: GARAMYCIN Injectable is contraindicated in individuals with a history of hypersensitivity or toxic reactions to gentamicin.

Warnings: Patients receiving treatment with GARAMYCIN should be under close clinical observation because of the toxicity associated with the use of this drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with preexisting renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with preexisting renal impairment. Kidney function diminished by infection of the upper urinary tract may, however, improve during effective treatment with GARAMYCIN Injectable.

Concurrent administration of potentially ototoxic drugs such as streptomycin and kanamycin or of potentially nephrotoxic drugs such as polymyxin, colistin, and kanamycin with gentamicin sulfate has not been shown to afford any clinical advantages and, moreover may result in additive toxicity. Monitoring of vestibular, cochlear, and renal function will provide guidance for therapy in such cases.

Precautions: In patients with impaired renal function in whom serious infection develops, serum concentrations of the drug may rise, with consequently increased risk of ototoxicity. In these patients or in those in whom recommended dosage or duration of therapy must be exceeded as a life-saving measure, routine studies of kidney function should be performed when possible. These may be supplemented by evaluation of the vestibular and auditory function and measurement of serum concentration of the drug when feasible. Serum concentrations of gentamicin should be maintained below the range of 10-12 mcg./ml. to reduce risk of ototoxicity.

Ordinarily, treatment should not be given for more than 7 to 10 days or be repeated unless required for serious infection not responsive to other agents.

As with other antibiotics, treatment with GARAMYCIN Injectable may occasionally result in overgrowth of nonsensitive organisms. If superinfection occurs, appropriate therapy is indicated.

Safety for use in pregnancy or the potential for fetal ototoxicity or nephrotoxicity have not been established. Studies in pregnant animals have not revealed teratogenic or ototoxic effects in the fetus. GARAMYCIN Injectable should not be used in pregnant patients or in women of childbearing age unless its use is deemed advisable by the physician.

Adverse Reactions: The overall incidence of ototoxicity considered related to treatment with GARAMYCIN Injectable was 2.8 per cent (16 of 565 patients). Contributory factors (two or more factors were relevant to most patients) were as follows: 10 had azotemia, 10 received a total of 1 gram or more of the drug, 7 had recently received other potentially ototoxic antibiotics (streptomycin or kanamycin), and 5 were over 60 years of age. Six also had decreased high-tone hearing acuity, which returned to or toward normal in the 4 patients retested.

Analysis of BUN data indicated that 4 (2%) of 172 patients showed increases in BUN that were probably related to treatment with GARAMYCIN Injectable. Of 20 increases probably or possibly related to treatment, 7 were reversible, 9 occurred in terminal patients, and 4 had no follow-up.

Other adverse reactions associated with treatment were one instance each of urticaria, decreased hematocrit, and reversible depression of granulocytes with normal bone marrow. Other rarely reported and possibly treatment-related adverse reactions were anemia, increased reticulocyte count, rash, purpura, drug fever, hypotension, convulsions, twitching, salivation, nausea, vomiting, increased transaminase activity (SGOT or SGPT), increased serum bilirubin, decreased serum calcium, and joint pain.

Packaging: GARAMYCIN Injectable, 40 mg./cc., 2-cc. multiple-dose vials, for intramuscular administration.

For more complete prescribing details, consult package insert or Physicians' Desk Reference. Schering literature is also available from your Schering Representative or Medical Services Department, Schering Corporation, Union, New Jersey 07083.

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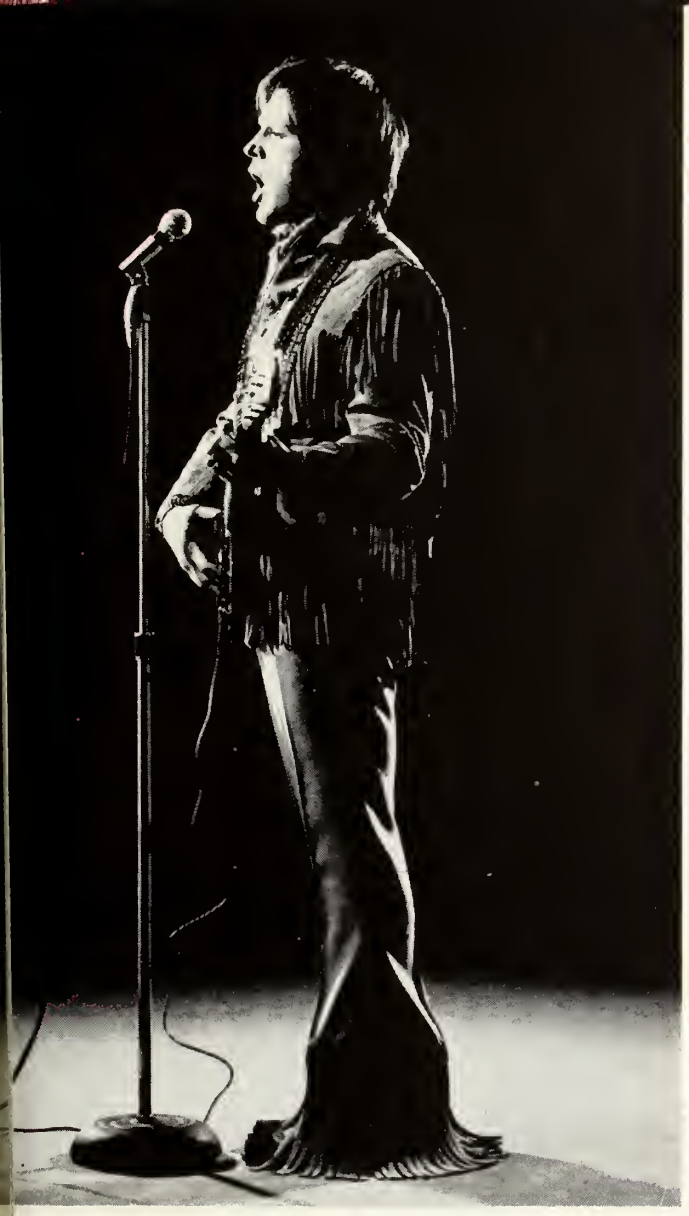

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a nonsalicylate analgesic equal to aspirin for the relief of pain,[1,2] yet unlikely to produce the irritation to the gastric mucosa so often associated with salicylate therapy[2]

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Prescribe PARAFON FORTE for effective spasmolysis and analgesia in sprains, strains, myalgias, low back pain, bursitis and other musculoskeletal disorders. Your patients will appreciate the restored comfort and freedom of movement it usually provides.

Contraindications: Sensitivity to either component. ***Precautions:*** Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped. ***Adverse Reactions:*** Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, *Paraflex* (chlorzoxazone) may possibly have been associated with gastrointestinal bleeding. While *Paraflex* (chlorzoxazone) and chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately eighteen patients, it was not possible to state that the dysfunction was or was not drug induced. ***Usual Adult Dosage:*** Two tablets q.i.d. ***Supplied:*** Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler, O. C., and Gyurik, J.: Industr. Med. Surg. *31*:372, 1962. 4. Forster, S., *et al.*: Amer. J. Orthop. *2*:285, 1960. 5. Friend, D. G.: Clin. Pharmacol. Ther. *5*:871, 1964.

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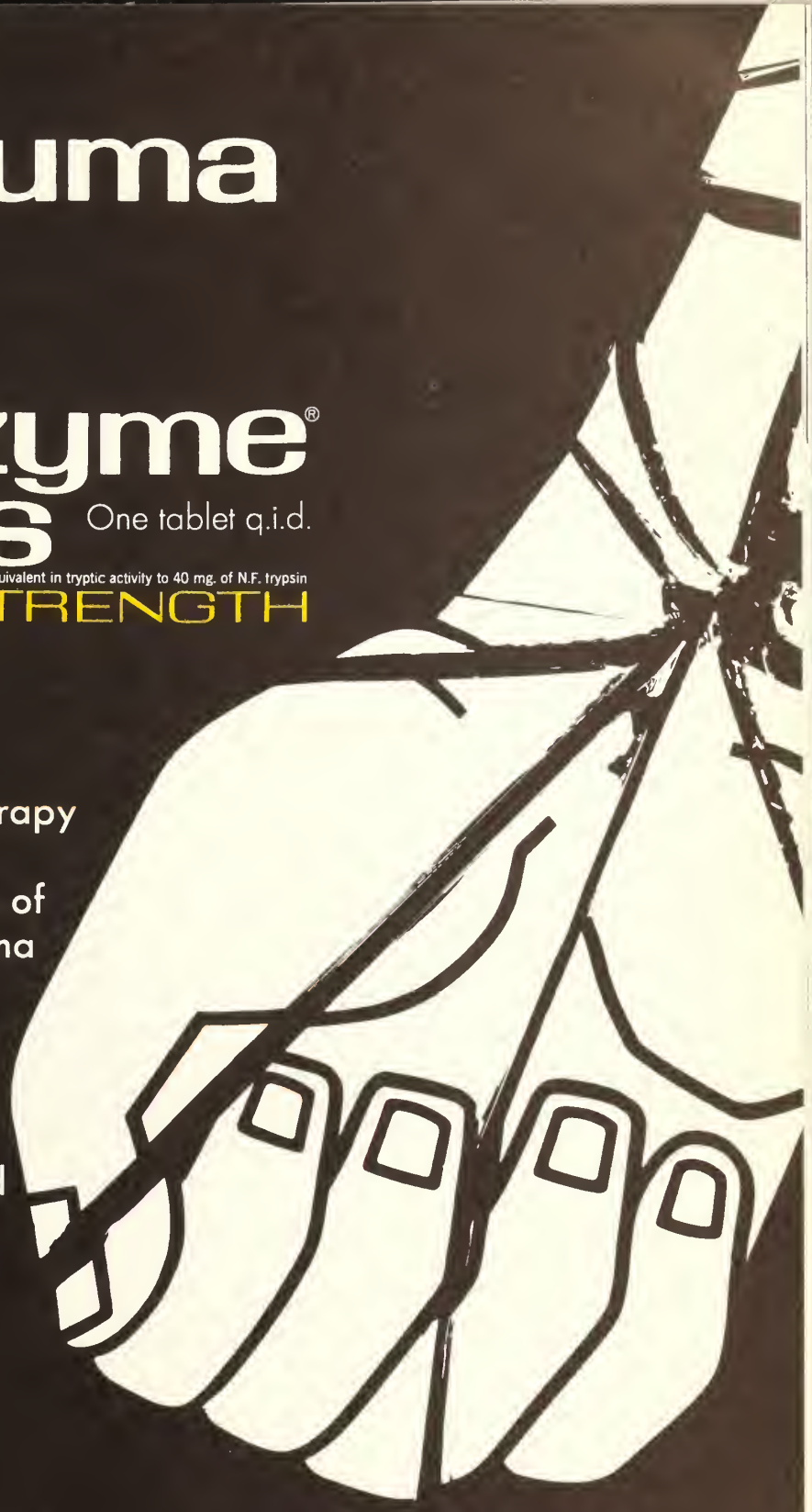

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- ☐ Postoperative Tissue Reactions.

Other conventional measures of treatment should be used as indicated. In infection, appropriate anti-infective therapy should be given.

Contraindications: ORENZYME BITABS should not be given to patients with a known sensitivity to trypsin or chymotrypsin.

Precautions: It should be used with caution in patients with abnormality of the blood clotting mechanism such as hemophilia, or with severe hepatic or renal disease. Safe use in pregnancy has not been established.

Adverse Reactions: Adverse reactions with ORENZYME have been reported infrequently. Reports include allergic manifestations (rash, urticaria, itching), gastrointestinal upset and increased speed of dissolution of animal-origin surgical sutures. There have been isolated reports of anaphylactic shock, albuminuria and hematuria. Increased tendency to bleed has also been reported but, in controlled studies, it has been seen with equal incidence in placebo-treated groups. (See Precautions.) It is recommended that if side effects occur medication be discontinued.

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Monilia emerging as a major therapeutic problem—
recent studies report increased incidence, attributed in part to the use of oral contraceptives,[1-4] broad-spectrum antibiotics[5-9] and prolonged use of corticosteroids.[7]
recent evidence establishes high rate of microbiological and clinical cure with AVC.[9-11]

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Dosage: One applicatorful or one suppository intravaginally once or twice daily.
Supplied: Cream—Four-ounce tube with or without applicator. Suppositories—Box of 12 with applicator.
References: 1. Gardner, H. L.: J. Miss. M.A. 8:529, 1967. 2. Porter, P. S., and Lyle, J. S.: Arch. Dermat. 93:402, 1966. 3. Walsh, H.; Hildebrandt, R. J., and Prystowsky, H.: Am. J. Obst. & Gynec. 93:904, 1965. 4. Vaginitis and the Pill: J.A.M.A. 196:731, 1966. 5. Guerriero, W. F.: South. M.J. 56:390, 1963. 6. Seelig, M. S.: Am. J. Med. 40:887, 1966. 7. To-day's Drugs, New York, Grune & Stratton, Inc., 1965, p. 316. 8. Gray, L. A., and Barnes, M. L.: Am. J. Obst. & Gynec. 92:125, 1965. 9. Salerno, L. J.; Ortiz, G., and Turkel, V.: Vaginitis: A Diagnostic and Therapeutic Approach, Scientific Exhibit, presented at the 115th Annual A.M.A. Convention, Chicago, Illinois, June 1966. 10. Walsh, J. C.; Sheffery, J. B., and Wilson, T. A.: Med. Ann. D.C. 37:35B, 1968. 11. Nugent, F. B., and Myers, J. E.: Pennsylvania Med. 69:44, 1966.

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Countersigned by:

President

Chairman of the Board

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(2) [illegible] ing whe[illegible] ice contract [illegible] rently in effect [illegible] Hos[illegible]

(3) [illegible] gins under th[illegible]

(4) [illegible] first enroll[illegible] Blue[illegible]

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If the service is an EKG or emergency accident care, please indicate on the "Explanation of Benefits," as we are unable to identify these two services from the "Explanation of Benefits" alone.

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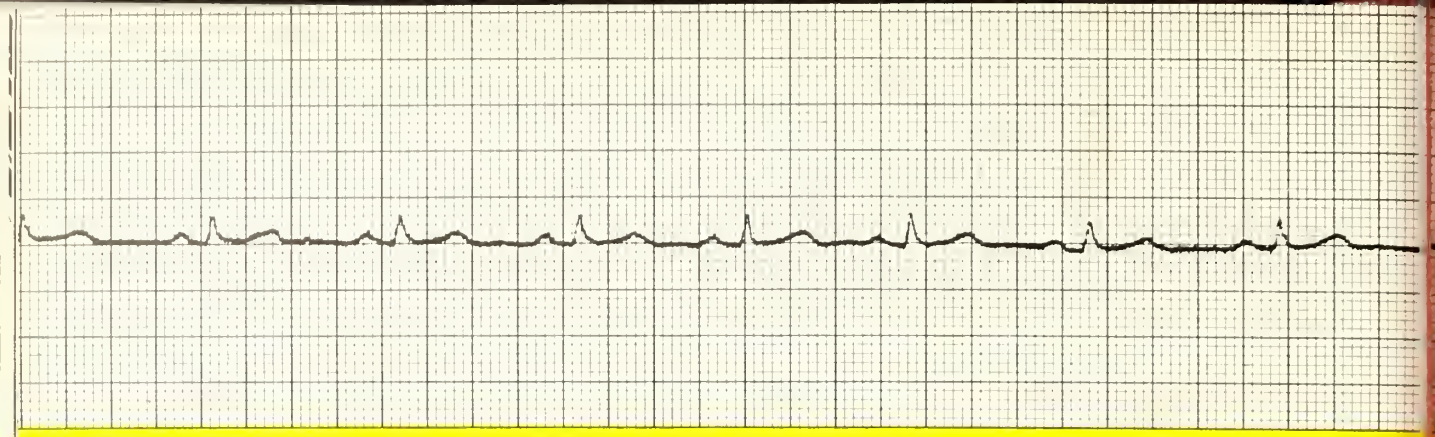

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms have occurred following abrupt discontinuance. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation, have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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THE JOURNAL
of
The Maine Medical Association

VOLUME 61 | SEPTEMBER 1970 | NUMBER 9

Maine Medical Center Number

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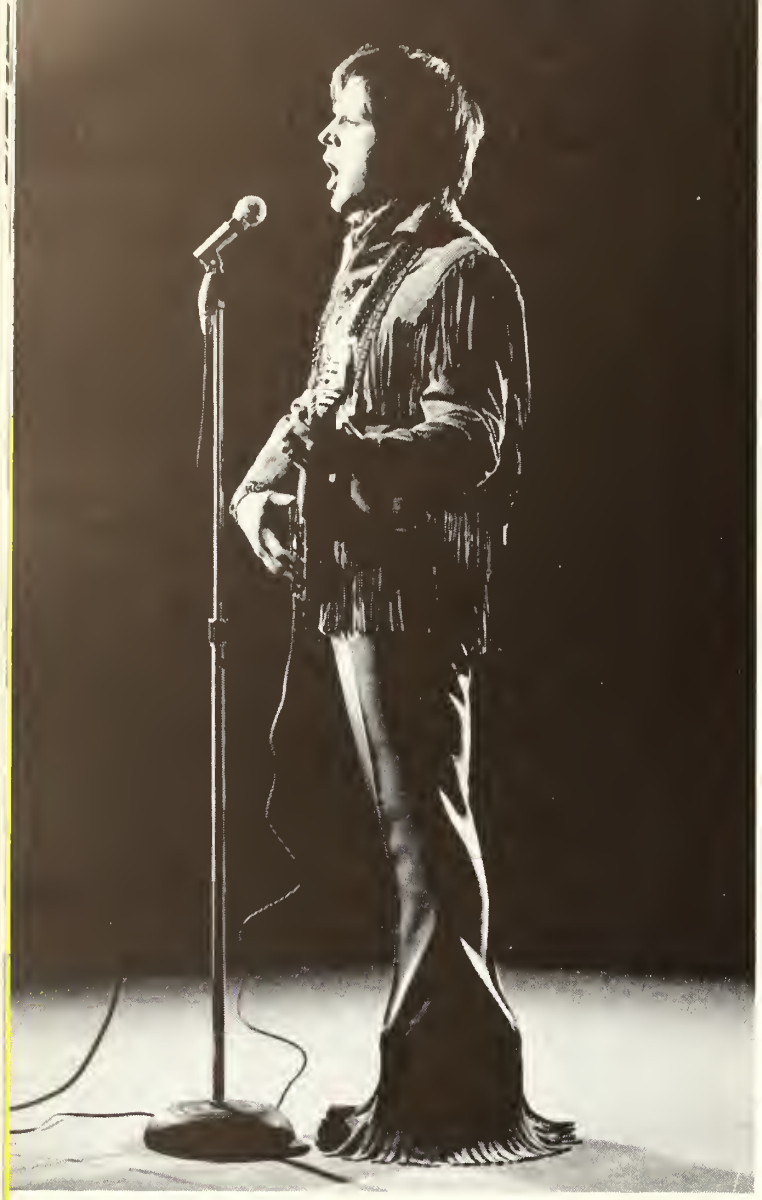

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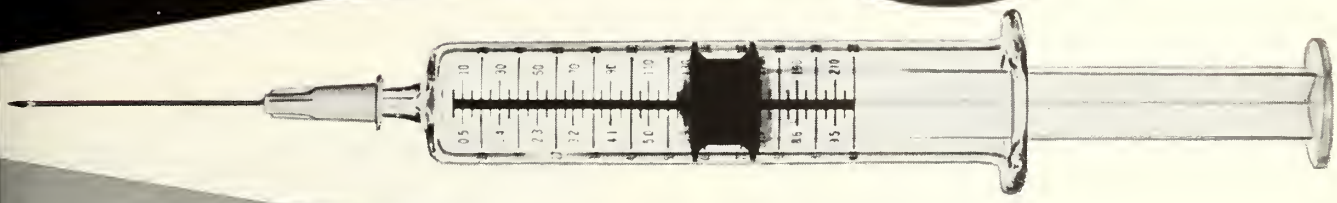

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* PATRICIA A. BERGERON, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.

Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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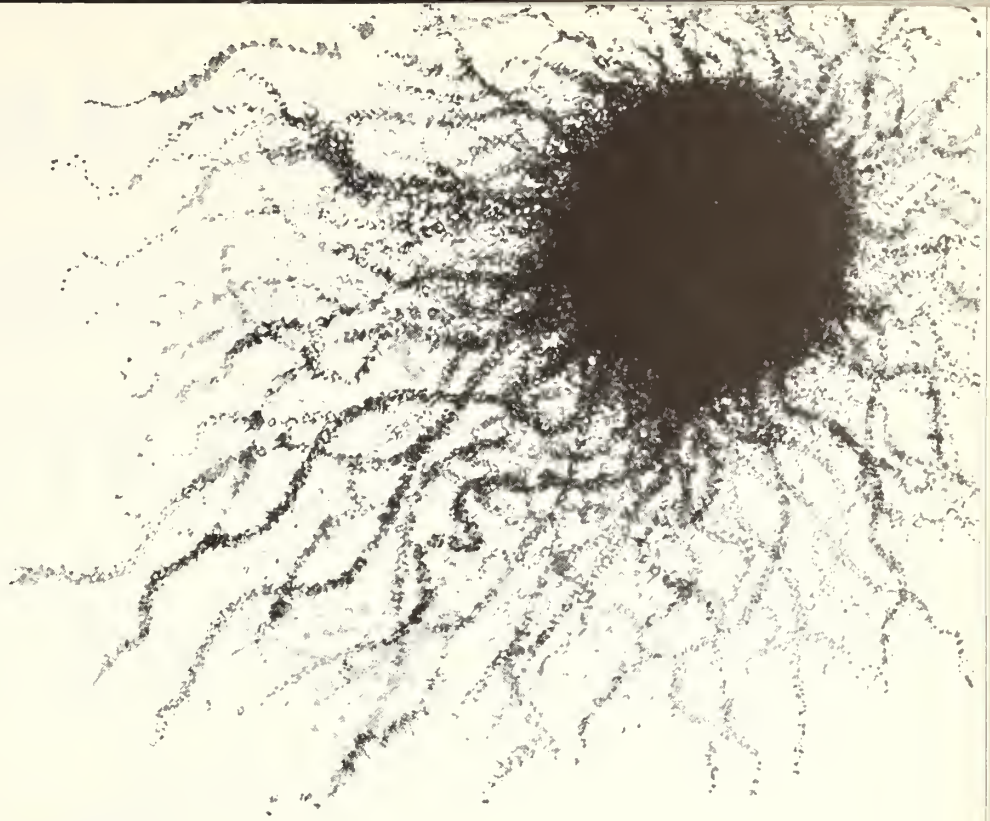

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Precautions: In elderly and debilitated patients, limit dosage to smallest effective amount of chlordiazepoxide (initially 10 mg or less per day) to preclude ataxia or oversedation; increase gradually as needed and tolerated. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects—particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in patients with impaired renal or hepatic function. Paradoxical reactions to chlordiazepoxide (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in the treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation very rarely reported in patients receiving Librium® (chlordiazepoxide) and oral anticoagulants.

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The Journal
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Volume Sixty-one | Brunswick, Maine, September 1970 | Number 9

Esophageal Rupture—A Catastrophic Complication of Vomiting

CLEMENT A. HIEBERT, M.D. and EUGENE GORAYEB, M.D.

Vomiting is one of life's more wretched moments. The prostrating nausea and abdominal straining, the reeking ferment cascading through mouth and nose is misery all out of proportion to the physiologic innocence of the event. Vomiting is the proclaiming act of the unwell. To hear that a patient has vomited is to hear only that he feels sick. Rare, indeed, must be the doctor who, for a single episode, allows himself to be rousted out of bed on account of it.

This paper is about two individuals who, in the spring of 1970, in losing the contents of their stomach very nearly also lost their lives. They did *not* feel better after vomiting. They felt far worse. In each instance, the esophagus had burst as a gastric tide erupted into the mediastinum and pleural spaces. Aroused from the experience of their care, signs and symptoms of so-called "spontaneous rupture of the esophagus" are herewith reviewed.

CASE REPORTS

Case 1 – A 60-year-old man was admitted to the Maine Medical Center after midnight on 2/20/70 with a history of having experienced indigestion the previous evening, for which he had taken Maalox.® Shortly after this, he vomited and was immediately smitten with sharp, mid-lower chest pain radiating to the back. His physician was called and noted a blood pressure of 84/60. The pain was partially relieved with narcotics and he was taken to the Emergency Ward of the Maine Medical Center.

His past history gave no indication of previous cardio-respiratory symptoms but he did have a long-standing problem with indigestion, heartburn, and occasional regurgitation.

On physical examination, he was found to be pale, dyspneic, and complained of pain in his chest. An electrocardiogram showed T-wave changes compatible with myocardial infarction. He was admitted to the Coronary Care Unit. X-rays taken soon thereafter, however, showed a pneumothorax to be present and a left trocar thoracotomy was done with removal of approximately 1,000 cc's of grayish fluid and a substantial amount of air as well. Partial reexpansion of the left lung ensued. He continued to have pain and review of his x-rays showed mediastinal emphysema to be present. It was then decided that he must be suffering from a rupture of his esophagus secondary to the vomiting, although radiopaque media introduced into the esophagus did not show a leak.

He was taken to the Operating Room on the night of his admission, approximately twelve hours after the onset of his symptoms. On opening his chest, it was apparent that he had sustained a total pleural burn, the surface of the lung and chest wall looked brown and partially digested. The mediastinal remnants of chicken pie were removed, the esophagus identified, and an inch long longitudinal esophageal tear just above the cardia closed. Because of the patient's antecedent symptoms of regurgitation and heartburn, his hiatus was then reconstructed in the fashion of a hiatal hernia repair so as to provide a proper angle between his esophagus and stomach, all of which was now restored to the abdomen and anchored.

Full expansion of his right lung was not attained until a rib resection and further drainage of the chest was carried out on 3/27/70, approximately five weeks after his original surgery. In addition to the problem of reexpanding his lung, he ate poorly and his normal weight, which was 175, fell to 145. Aided by a "life line" intravenous high calorie alimentation, he improved slowly and steadily. His chest x-ray and barium swallow were normal and his wounds were healed at the time of discharge on 4/10/70. He has remained well and free from symptoms, without the chest complaint predating his surgery.

Case 2 – A 41-year-old man was admitted on 5/5/70 to the Emergency Ward of the Rumford Community Hospital at 7:30 A.M. For one and one-half weeks prior to admission, he had experienced an increase in his "chronic sour stomach and heartburn," for which he had used Maalox for years. He had never seen a physician previously for this trouble or had he x-rays to determine the nature of the malady. On the day prior to admission, he had had a bout of diarrhea, with nausea, followed by vomiting of black material. *Immediately* thereafter, he had a "knot in the pit of his stomach." It was sufficiently painful that he was taken to the Emergency Room of the Rumford Community Hospital where he was found to be pale, cold, and clammy. His blood pressure was 80/30. Examination revealed boardlike rigidity of the upper abdomen, but flat plate and upright film of

chest and abdomen were entirely normal except for question of a pneumonic process in the left lower lobe. The initial diagnosis of a perforated peptic ulcer was changed to pneumonia of the left lower lobe after a Levin tube was inserted with relief of his abdominal pain and disappearance of its rigidity.

Laboratory studies included a WBC of 16,000, a normal hemoglobin and hematocrit, and normal amylase.

He was treated in the Intensive Care Unit with intravenous alimentation and Polycillin,® 500 mgs. q6h.

X-rays on the day following admission showed a massive left-sided pleural effusion and 1,000 cc's of fluid was removed from his left chest. Again on the second hospital day fluid and air were present and a diagnosis of empyema and pneumothorax was entertained. Closed thoracotomy at the second interspace in the mid-clavicular line was carried out and a further 900 cc's of fluid was removed. On the fifth postoperative day, an additional closed thoracotomy in the posterior axillary line was carried out with further reexpansion of his lung. He was allowed to eat, his temperature, which had been in the range of 102 to 104, gradually subsided and he was much less dyspneic. With oral fluids, however, the output from his chest catheter increased to 6,000 cc's daily.

At this point, the diagnostic possibility of a ruptured esophagus was suggested and confirmed by a barium swallow.

Oral intake was stopped and IV hyperalimentation was started. Repeated x-rays have since shown gradual closure of the esophageal fistula but he has continued to have a 10% pneumothorax with pleural thickening.

Now, two months after admission, he is again able to take oral liquids with most of it passing into his stomach. His temperature remains normal and his wounds are healing slowly. Weight loss since admission is approximately fifty pounds. He has received two blood transfusions. Except for a continued white count in the range of 15,000, his laboratory studies, including electrolytes, serum protein, and hemoglobin, have been within normal limits.

Comment

Each of these patients was first thought to have something else. In the first instance, chronic gastroesophageal reflux had probably mimicked angina, and the patient was initially thought to have had a myocardial infarction. With the second patient, physical findings suggested a perforated ulcer and x-rays indicated pneumonitis. In both cases, air in the pleural space became apparent and the diagnosis was switched to spontaneous pneumothorax. In retrospect, the true condition was all too apparent. But at the time, vomiting was regarded only as a symptom. not as a *cause* of the associated events. *To make the diagnosis of a ruptured esophagus, the condition must be thought of when pain and prostration follow vomiting.* A careful history is indispensable.

When early diagnostic clues are missed, the patient's dyspnea and pain will worsen. Myocardial infarction, pulmonary embolus, perforated ulcer, and dissecting aneurysm can usually be excluded by the electrocardiogram and x-ray findings. Verification of the rupture may be obtained with a swallow of water-soluble contrast material or thin barium. Perforation usually occurs on the left side of the esophagus just above the diaphragm. Successful primary repair depends on prompt diagnosis and expeditious surgery. Concomitant gastrostomy, Levin tube drainage of the esophagus, and IV hyperalimentation are important supportive measures.

One is tempted to speculate that in each of these two patients primary incompetency of the gastric cardia may have been the predisposing condition by 1) accommodating a large and sudden flooding of the gullet with gastric contents, and 2) by initiating the catastrophic vomiting through irritation of the lower esophagus in the first place. Other authors have discussed the role of esophagitis in mechanically weakening the esophageal wall and thereby predisposing to spontaneous rupture.[1,2,3]

That an otherwise normal organ may burst with the vomiting is attested to by the celebrated description by Boerhaave[4] in 1724 of Baron Wassenauer's prodigious last meal which consisted of: white cabbage boiled with sheep, spinach, roast calf, sweet breads, the thigh and breast of a duck, two larks, apple compote, bread, pears, grapes, and sweetmeats washed down with beer and wine!

Summary

Two patients with spontaneous vomiting and concomitant esophageal rupture are presented and the syndrome of esophageal rupture is discussed. Prompt diagnosis is crucial and depends primarily on a history of prostration and severe chest or epigastric pain *following* vomiting. Confirmation is by x-ray and the treatment is surgical.

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Isolated Mesenteric Lipodystrophy

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INTRODUCTION

The condition of isolated mesenteric lipodystrophy, which has been called also lipodystrophy of mesenteric fat, is characterized by the unusual appearance of the mesenteric fat and marked thickening of the mesentery of the small bowel. The etiology of this relatively rare condition is unknown. Interest in isolated lipodystrophy of mesenteric fat arises from the fact that it presents problems in diagnosis, in differentiation from the conditions which cause the vague abdominal pain, low grade fever, and discomfort, particularly in distinguishing it from malignancy.

Therapy when indicated is surgical resection or biopsy alone when necessary to save intestinal blood supply. Only two cases have been noted at the Maine Medical Center in the past 11 years with the pathological description. Few cases have been previously reported as mesenteric lipodystrophy, and it may be observed with increasing frequency.

CASE REPORTS

Case 1. E.M., a sixty-seven-year old man, had experienced left flank pain without localized tenderness for one and a half years. Initially the pain was relieved by hot packs, but gradually it became excruciatingly severe and sudden left abdominal pain with occasional penile radiation, which was sufficient to preclude sleep and was relieved by a tablet of Demerol®. The patient was admitted to the Maine Medical Center in February 1957, for study. Physical examination was not significant except for slight tenderness over the sigmoid colon associated with hyperactive peristalsis, nausea and vomiting. No mass was palpated. Routine blood determinations were within normal limits. Six stool examinations for occult blood were negative. X-ray showed arthritic changes in the lumbar spine and pelvis. Intravenous pyelogram and barium enema were negative. Upper GI series showed an easily reducible hiatal hernia. After symptomatic treatment, the patient was discharged.

Two months later, he developed a small spot of burning pain beneath the twelfth rib with intermittent left flank and para-umbilical pain. Neurologic examination revealed some cutaneous hyperesthesia corresponding to the area of his pain and over the posterior aspect of the same dermatome. The impression was that of left intercostal neuritis perhaps due to spinal cord or osseous spinal disease. The pain seemed to be relieved symptomatically by a posterior intercostal block, but the patient complained of rectal tenesmus with bleeding. He underwent sphincterotomy and bowel movements became comfortable. However, the operation did not produce any improvement in the abdominal complaints.

The patient was admitted again for abdominal exploration in August 1957. At operation, a doughy, firm mass approximately the size of the two closed fists was encountered within the substance of the mesentery of the jejunum. It was contiguous to some of the loops of the small intestine, but did not seem to encroach upon, or invade, the musculature of intestine, nor to interfere with its blood supply. The mass was removed and the pathology was characteristic of isolated mesenteric lipodystrophy. In addition to this large tumor, there were several smaller satellite nodules — 1 to 2 cm in diameter — which felt like enlarged mesenteric lymph nodes Figs. 1 and 2.

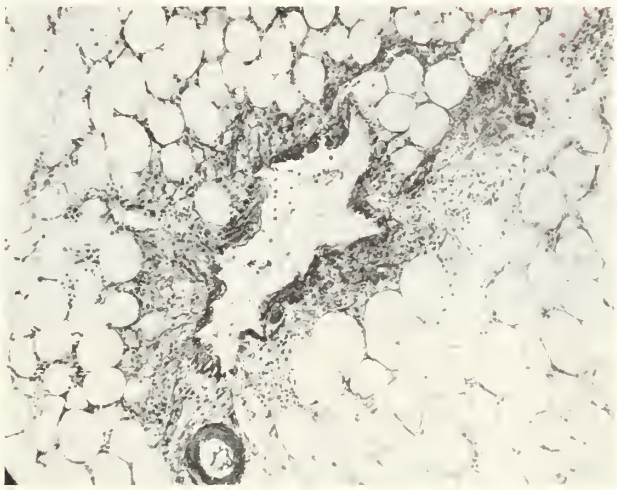

Fig. 1

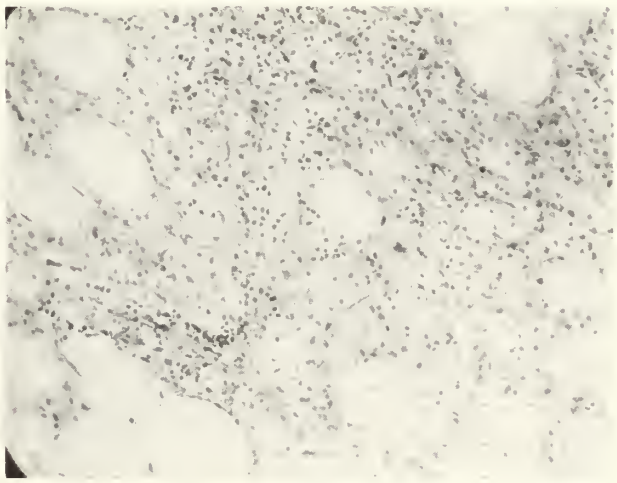

Fig. 2

Following this operation, he was well until April 1958 when he had idiopathic left femoral neuritis. He died in July, 1964, with cerebral thrombosis and bronchopneumonia. No autopsy was obtained.

Case 2. M.J., a sixty-nine-year old white female was admitted on November 30, 1967, with epigastric distress which was characterized by indigestion, heartburn, dysphagia and substernal discomfort. Previous x-rays in 1960 showed gallstones and in 1966 a diaphragmatic hernia. She had lost 20 pounds in one year and subsequently her blood pressure was reduced from 220/110 to 160/90. There was low grade fever.

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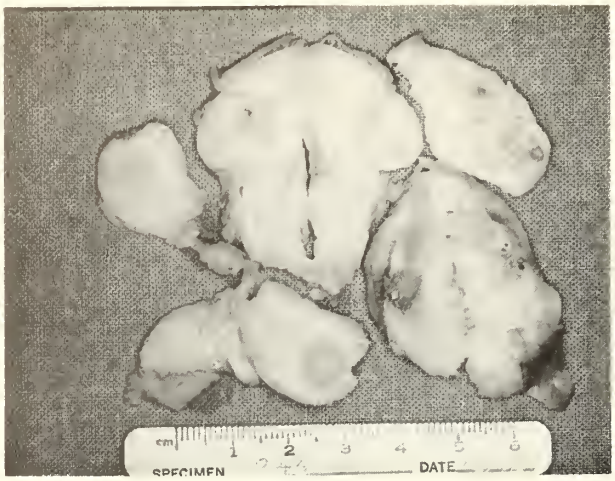

Fig. 3

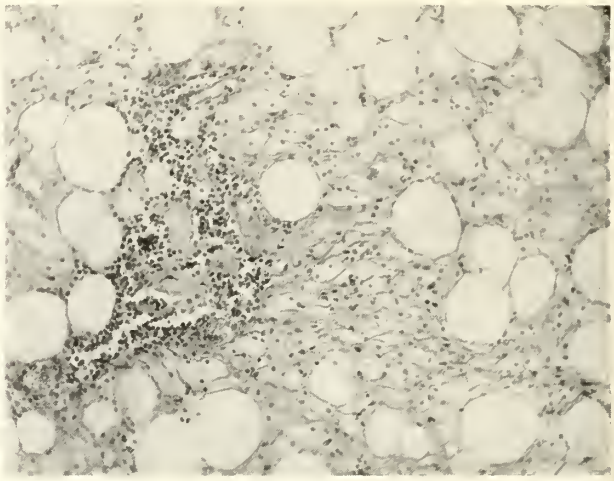

Fig. 4

Physical examination was not remarkable. The patient was treated for severe coronary heart disease in 1960 but since that time she had had no complaints referable to her coronary disease. No heart murmurs and no abdominal masses or tenderness were noted.

Under the impression of symptomatic diaphragmatic hernia and chronic cholecystitis with cholelithiasis, she had a cholecystectomy, repair of diaphragmatic hernia and splenectomy with drainage of a large left renal cyst. Two days after surgery the patient died from progressive cardiovascular decompensation. Autopsy revealed septal myocardial infarction secondary to coronary arteriosclerosis. The peritoneum appeared dull and edematous with small amounts of brownish fluid in the cavity. Both kidneys showed several cysts variable in size. The mesentery of the small bowel was boggy and thickened up to 7 cm. The cut surface revealed scattered areas of tan brown discoloration of fat with some enlarged lymph nodes. The celiac and mesenteric arteries did not show any evidence of occlusions. Microscopic examination of the fat was characteristic of isolated mesenteric lipodystrophy Figs. 3 and 4.

Pathology: Grossly, the mesentery is markedly thickened and the normal lobulations of fat are lost with discoloration. The thickest portion is central and thins out somewhat peripherally. The diffusely involved mesentery shows rubbery firm discoloration which varies from non-greasy yellow brown to pale yellow. The size of nodules vary from 7.0 to 1.0 cm in diameter. The small bowel itself appears normal and mesenteric vessels show no evidence of thrombi.

Microscopically, the mesenteric nodules show mild to moderate infiltration of the altered fat cells by macrophages with foamy cytoplasm. In the center of some nodules, there is a relatively normal lymph node or blood vessel around which there are occasional normal fat cells, surrounded by various layers of abnormal fat cells. The abnormal fat cells are smaller than normal. The cytoplasm is finely granular with one or two small vacuoles probably presenting neutral fat. The nucleus is small and round and is placed centrally or slightly eccentrically.

Occasionally there are focal collections of lymphocytes usually adjacent to small vessels without follicle formation. Also, there are small amounts of fibrosis in scattered areas of the abnormal fat. With the Oil Red O stain, the abnormal fat cells are paler than normal fat cells which are stained homogeneously deep red, and there are a few needle-like crystals with occasional Maltese cross noted under polarizing microscope. There is no vasculitis or giant cells.

Comments

In 1947, Pemberton described this condition as an early stage of Whipple's disease, but later he felt that this interpretation might be incorrect. In 1955, Crane and associates agreed with the concept of Pemberton and called the condition isolated lipodystrophy, describing five cases. Farris added one more case in the discussion of their report. In 1960, Ogden and co-workers reported similar findings as Panniculitis of the mesentery with a review of seven cases. In 1961, Rogers and his associates introduced one case involving the mesentery, small intestine and retroperitoneum. In 1962, Tedeschi concurred with the suggestion of refractile mesenteritis which was originally described by Jure in 1924. In 1966, French and his co-worker described 14 cases fitting the criteria of this so-called lipodystrophy of mesenteric fat. They suggested that the first report was that of regions of doubly refractile fat like substances in the mesentery described by Schlagenhauser in 1907.

Summary

Two cases are presented of a condition described as isolated mesenteric lipodystrophy which were observed at the Maine Medical Center during a period of 11 years. One of these cases was observed at operation and removed with subsequent improvement of the patient's symptoms. The other case was observed as an incidental finding at autopsy in a patient who died of cerebral thrombosis. A review of the literature concerning this condition and a description of the pathologic findings are reported. The long survival of the first patient following establishment of the diagnosis at operation emphasizes the favorable prognosis in these cases.

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Chronic Renal Disease in Maine*

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Although the principle of hemodialysis was described in 1913,[1] it did not become therapeutically feasible until 1945.[2] At this time, Kolff constructed a kidney in Holland during the German Occupation and treated several patients with hemodialysis. Subsequently, during the 50's various types of kidneys were designed principally to treat patients with acute renal failure. With the advent of the arterial-venous shunt,[3] long-term dialysis became a reality and since 1960 the use of dialysis and transplantation has been a feasible therapeutic measure.[4]

The process of dialysis simply involves removal of unwanted elements from the blood by diffusing them through a cellophane membrane from the blood into an electrolyte bath solution. The construction or design of the kidneys may vary; however, they fall into two general categories: a) the coil type kidney and b) the parallel flow dialyzer. Largely through the work of Dr. John Merrill,[5] the coil dialyzer has gained great acceptance and has the advantage of being easy to handle, disposable, and relatively simple to operate. In 1967, it became apparent to many people interested in kidney diseases that a good number of patients were dying because of lack of proper facilities. At that time, the U. S. Bureau of Budget commissioned the Gottschalk Committee to investigate renal disease throughout the country.[6] The report indicated that approximately three to four people out of every 100,000 were candidates for hemodialysis. Since that time, numerous (as yet unpublished) studies[7] indicate that the need is far greater than what was originally anticipated. Some investigators feel that there may be as many as fifteen people per 100,000 who are candidates for dialysis and possibly transplantation. A more realistic figure, in our estimation, is that of approximately five patients per 100,000 or fifty patients per 1,000,000 are suitable for treatment and can be rehabilitated through the means at hand. A survey conducted at the Maine Medical Center in 1967[8] showed that we were seeing, just in the hospital, somewhere between 25 and 30 patients who were suitable for dialysis and/or transplantation. At that time, we had neither the means nor the financial backing to undertake such a program. The unfortunate aspect of the problem was that many of these patients could be rehabilitated and returned to a normal life. Further investigation throughout the past six months shows that the State of Maine is generating fifty patients per year who could be considered as ideal candidates for dialysis and/or transplantation therapy. We believe this figure to be a conservative one. In the past, most patients having a kidney disease were referred to Boston or some major center for therapy; however, during the past year and a half, the larger centers have been unable to accommodate all of our patients. For these reasons, we felt a moral obligation to establish a program for the citizens of the State of Maine to care for their needs. With the help of our Governor, State Legislature, the hospital staff and administration, the Regional Medical Program and private citizens, we were able to acquire funds, space, and support for a dialysis unit to care for fourteen patients with chronic renal disease. In time, this number can be doubled by increasing the number of shifts during which dialysis is undertaken.

The purpose of the communiqué is to inform the physicians of the State of Maine that facilities are becoming available to help our citizens, and to seek out professional personnel within the State who might be willing to start dialysis units and care for dialysis patients at home in some of the more remote portions of the State. We are most interested in a cooperative venture which is statewide in scope.

In the two and a half years of planning and working with chronic disease programs, we have encountered a number of situations which hopefully would benefit anyone wishing to embark on a dialysis program. First and foremost, we have found that it is very important for a hospital interested in dialysis to tailor its particular program to suit the needs of its community and available physical structures. It is well, necessary and useful to have outside help and advice; however, as has been reported,[9] what is appropriate for one hospital is not necessarily suitable for another. Unfortunately there is no magic formula for setting up a dialysis unit nor is there a standard "Protocol" which covers all of the problems which might arise. In fact, our personal observation is that strict adherence to protocol tends to diminish original thinking and degenerates treatment into a "cookbook procedure" which may in turn lead to poor patient care. Another stumbling block in the development of a dialysis/transplant program is to be found in the form of a "Lay Professional Organizer." Again, personal experience has been that this approach creates more problems than it solves. We have also become aware of the fact that the people most intimately involved with patient care are in a better position to outline the needs of the patients and the dialysis/transplant unit.

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We hope that the physicians of Maine will make use of the facilities soon to be available, and we offer our assistance not only in taking care of patients but in setting up programs in other areas.

Currently there is some disagreement as to the acceptability of a patient with chronic renal disease for dialysis. Some general guidelines can be put forth which may be helpful. We feel that most patients suitable for dialysis are under the age of 65 and have no other major illnesses except those secondary to the kidney disease itself. A willingness to undertake such a program is extremely important.

Regarding transplantation, the restrictions are more stringent. Suitable patients are under the age of 45, but need not have a related donor. It is our feeling that, although the financial considerations are great, no patient should be denied treatment because of lack of funding. There are insurance policies, Blue Cross/Blue Shield, State and Federal Funds which can be used to help to ease the financial burdens. The mechanisms for proper funding have not been completely outlined, but will be clarified in the near future. Many new ideas concerning this were generated at the New England Regional Program for End Kidney Diseases held on June 25th in New Hampshire.[10]

This report simply represents a beginning of what hopefully will become a more comprehensive program, and we invite suggestions, criticisms and questions from any interested physicians within the State.

Summary

This is a brief outline of the facilities for the care of end stage kidney diseases in the State of Maine. Emphasis is placed on the fact that this is a state-wide program, and it is designed for all patients who are medically suitable for treatment. It is also emphasized that we are willing and eager to cooperate with physicians and hospitals within the State in the care of patients or in the construction of dialysis units in other areas.

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Consumption Coagulopathy Associated With Abdominal Aortic Aneurysm

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The syndrome of disseminated intravascular coagulation is now recognized as the cause of a bleeding diathesis in a variety of disease states.[1] Once referred to as "the defibrination syndrome,"[2] the term intravascular coagulation or consumption coagulopathy seems more appropriate as it refers to the basic cause of the bleeding diathesis although not the specific etiology. Significant intravascular activation of the clotting mechanism leads to disseminated intravascular coagulation with depletion of fibrinogen, platelets, and other labile clotting factors; and to the activation of the thrombolytic system with the appearance of fibrin-split products (FSP), which through their anticoagulant properties, contribute further to this generalized bleeding tendency.

We recently had the opportunity to study a patient admitted for elective surgery of an abdominal aortic aneurysm who had a history of bleeding tendency. The results of this study, the response of Heparin® therapy, and the ultimate correction of his coagulation abnormalities by removal of the aneurysm suggest an acquired hypofibrinogenemia with fibrinolytic activity secondary to consumption of coagulation factors within the aortic aneurysm.

PATIENT SUMMARY

M. G., 75-year-old male, second Maine Medical Center admission, Admission – 10/6/69, Discharge – 11/18/69.

This 75-year-old male was admitted for evaluation of a pulsating abdominal mass. The mass had been known for about one year and the patient was unaware of any change in its size. He denied back pain or symptoms suggesting intra-abdominal bleeding.

Past History – The patient had sustained traumatic amputation of his left foot in 1915. An elective hernia repair was done in 1940 without incident. In October 1964, he had an acute myocardial infarction with characteristic EKG and enzyme changes; and was maintained on anticoagulant therapy, with warfarin sodium, for the next three and one-half years.

His first admission to the Maine Medical Center was in September of 1968 for evaluation of a chronic ulcer on the dorsum of his tongue. This lesion had not responded to diathermic coagulation. Because of an extensive subcutaneous hemorrhage, his anticoagulant had been discontinued three months prior to this admission. Coagulation studies at this time showed a Lee-White clotting time of 10-19-24 minutes, decreased blood platelets by peripheral smear, a P-time of 29.5% or 19 seconds, and a normal partial thromboplastin time (PTT). He was taken to the operating room and the tongue lesion excised. Post-op he bled extensively despite large amounts of parenteral Vitamin K. Six units of blood were required, two of these fresh, to finally control the hemorrhage. Bleeding studies at the time of his discharge from that admission were essentially unchanged. No mention was made of the presence of the abdominal mass during this admission.

Family History – Non-contributory; specifically, there was no history of bleeding tendency.

Physical Examination – The patient was a well-developed, well-nourished male of his stated age; Temperature 98.6, Pulse 60 and regular, Respirations 19, and Blood Pressure 190/90. The positive findings on examination were as follows: The eyes showed bilateral arcus senilis. There were upper dentures, and extensive dental work in the lower jaw. The tongue showed a small scar on the dorsum which was well-healed. The carotid pulses were widened, but no bruit was heard. The chest showed increased AP diameter with decreased breath sounds, but otherwise clear to auscultation and percussion. There was slight cardiac enlargement with the apex outside the anterior axillary line; no murmurs were heard. A fist-sized pulsating mass was found in the upper abdomen with a diameter of 9 to 10 centimeters extending from the left flank to the right anterior abdomen. There were normal femoral and popliteal pulses. There was an amputation of the left leg and foot below the knee, with the stump being well-healed.

Hospital Course – Laboratory studies showed a hemoglobin of 10.5 grams, and a hematocrit of 34. The white blood cell count was 7,076 with a normal differential. The red blood cells appeared hypochromic and platelets seemed reduced. The platelet count was 82,000 and the P-time was 24.5% or 20.5 seconds. Lee-White clotting time was 14-18-24 minutes, and PTT (activated) was 55 seconds (control 36 seconds). Blood chemistries and electrolytes were normal except for a blood urea nitrogen of 24 milligrams percent. The plasma fibrinogen was 30 milligrams percent and the serum was positive for fibrin-split products. Bone marrow examination was normal.

A chest x-ray showed a mild left ventricular enlargement and the abdominal film showed a large aneurysm of the abdominal aorta, 9 centimeters in width and 15 centimeters in length. The electrocardiogram showed sinus bradycardia, left axis deviation, Digitalis effect, and an old superior infarction.

A diagnosis of probable acquired hypofibrinogenemia secondary to a consumption coagulopathy was made and the patient was treated with Heparin 5,000 units intravenously every 6 hours. During the next 10 days, his coagulation studies were carefully monitored (see chart). On 11/1/69, after all the studies had returned towards normal, he was taken to the operating room, given 4 grams of fibrinogen and an abdominal exploration was done.

At surgery, no abnormal bleeding was experienced in opening the abdomen. The aneurysm was identified and dissected free as were the iliac vessels. There was a left common iliac aneurysm as well. Because of the known bleeding tendency, a small woven 22 mm. Dacron prothesis was used after excision of the aortic and left common iliac aneurysms. Bleeding did become somewhat brisk and during the 6-hour and 45-minute procedure, six units of fresh whole blood were used. The abdomen was not drained and his immediate postop status was good. There was no unusual bleeding from the skin edges and satisfactory femoral pulses were present.

His post-op course was carefully followed without evidence of hemorrhage. Other than two transient episodes of atrial fibrillation, requiring rapid supplementary doses of Lanoxin,® and a mild increase in his BUN, his course was benign. His coagulation studies are recorded (see chart) and continued to be nor-

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Summary of Coagulation Studies

DATE		10/6/70 Adm	10/7	10/4	10/17	10/21	10/28	10/31	11/1 Thru 11/5	11/6	11/12	11/18 Discharge	12/18
TREATMENT	NORMAL VALUES			Heparin →				Surgery					
Fibrinogen (mg%)	200 – 400	30	30		150	246	240	381	250–300	210	250		240
Platelets	250,000 – 300,000	82,000	100,000		84,000	180,000	58,000				292,000		250,000
P-Time	13 sec/100%	20/24	21/26		16/56	20/24					15/74		15/74
P.T.T (Activated)	35 – 50 sec	55	52		62	90					48		
P.T.T Control		36	31		31	33					43		
Fibrin Split Products (mg%	0	40	42		26	22	12	6		0	0		0
Clotting Time Lee – White	15 – 18 min	10 18 24		over 1 hr		24 36 42	24 30 36				10 15 18		

mal. There was a disappearance of the fibrin-split products from the serum over the next 5 days. The Heparin therapy, which was terminated at the time of his surgery, was not resumed.

At the time of surgery, the aortic aneurysm was not grossly filled with fibrin and thrombus. However, the microscopic sections showed the aneurysm wall to be made almost entirely of collagen and adherent fibrin and thrombin.

The patient has been checked periodically since surgery and is alive and well. His current coagulation studies have remained normal (see chart).

Discussion

The case described satisfies the criteria for the diagnosis[3] of a consumption coagulopathy with increased fibrinolytic activity. The low fibrinogen level, low blood platelet count, and the presence of FSP in the serum, all corrected temporarily by Heparin therapy, and permanently by removal of the aortic aneurysm, are diagnostic in themselves. However, the abnormal PTT and P-time also suggest depletion of the other labile coagulation factors, i.e., factors V, VIII, and XIII. Assay studies were not available to us, hence, only indirect evidence of their depletion was available. One finding which is usually seen in this syndrome was not present in our case. This was the presence of fragmented and bizarre-shaped red blood cells – so-called schistocytes.[4] These were carefully looked for and a few were found; however, their number did not appear increased. The results of Heparin therapy were consistent as far as the fibrinogen, blood platelets, and FSP, but not necessarily the PTT and the P-time. This is not unusual and others[5] have called attention to this fact. It is also possible that the anticoagulant effect of Heparin itself influenced the results of these tests.

An intriguing aspect is the speculation regarding the mechanism involved in this particular case. There probably were several important factors. First, was the stagnation of blood within the aneurysm itself. Next, may have been the damaged endothelial wall to which platelets adhere rapidly and activated the coagulation system, mainly the intrinsic pathway. Now fibrin was being formed within the aneurysm, and this initiated the fibrinolytic system with the development of the FSP. It is known that these breakdown products of fibrin excite an anticoagulant action by: (1) the inhibition of an orderly polymerization of fibrin monomer to fibrin resulting in a faulty clot, (2) a direct antithrombin effect, (3) forming unclottable complexes with fibrin monomer, and (4) an inhibition of platelet aggregation.

One might have expected to see large amounts of fibrin within the aneurysm removed, and this was our first impression, as this is not an unusual finding at the time of surgery. However, this patient was treated for over two weeks with Heparin which certainly could have modified the amount of fibrin present. The microscopic sections confirm the presence of fibrin in large amounts within the wall of the aneurysm. Although not a large search of the literature has been made, the association of this syndrome with an aneurysm has not been publicized widely. Personal communication[6] reveals others have encountered this phenomena, but usually in the face of active bleeding associated with an aneurysm.

Summary

The authors have reported a case of abdominal aortic aneurysm associated with the symptoms of consumption coagulopathy. The bleeding tendency and the abnormal coagulation studies were permanently corrected by the excision of the aneurysm.

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Traumatic Rupture of the Normal Aortic Valve

A Case Report and Review of Subject

CHRIS A. LUTES, M.D.* and BERNARD GIVERTZ, M.D.**

Non-penetrating chest trauma often results in injury to the heart which may vary in severity from rapidly fatal cardiac rupture to asymptomatic lesions detectable only by serial electrocardiograms or serum enzyme determinations.[1] It has been estimated that as many as 38% of patients sustaining chest injuries may also show evidence of cardiac damage.[2] Although isolated cardiac valve lesions have been relatively uncommon after blunt trauma,[3] when they do occur they most often involve the aortic valve.[4] The following case is a rare example of this lesion and illustrates current therapeutic management.

CASE REPORT

N.H., a 32-year-old white, married male was involved in an auto accident 48 hours prior to admission to the Maine Medical Center. He sustained multiple injuries including abrasions of the legs, face and right anterior chest, lacerations of both lips, a fracture of the right clavicle and right first rib, and a comminuted fracture of the right femur. The morning following the accident he was alert and taking fluids without difficulty. His minor injuries had been cared for and he was seen in consultation for treatment of his fractured femur. Physical findings consistent with severe aortic insufficiency were found and the patient transferred to the Maine Medical Center for further evaluation. He was alert, cooperative and asymptomatic at rest. A right Horner's syndrome was present. Blood pressure was 180/40/0 and pulse 110. Typical pistol shot pulses were present. The cardiac impulse was active and the aortic second sound was absent. A Grade V/VI diastolic decrescendo murmur was audible over the aortic area and along the left sternal border. Hemoglobin was 15.7 Gm., WBC 20,000 with 86% polys. Clotting factors were normal. Bilirubin 1.1 mg.%, serum creatinine 1.4 mg.%, BUN 42 mg.%. Transaminase 136 mg.%. Blood type AB negative. X-rays demonstrated a fracture of the right clavicle, the first rib, and a comminuted fracture of the midshaft of the right femur. The heart and lungs were within normal limits. Changes consistent with left ventricular hypertrophy and digitalis effect were present on the ECG. The day after admission cardiac catheterization including cineangiography demonstrated massive aortic insufficiency. Right heart pressures were normal except for an "a" wave of 19 mm Hg. in the pulmonary artery wedge pressure tracing. The left ventricular end diastolic pressure was 25-30 mm Hg. The finding of a higher end diastolic left ventricular pressure than pulmonary capillary "a" wave pressure was indicative of premature closure of the mitral valve, a hemodynamic finding described in severe sudden aortic insufficiency.[5,6,7] There were no other cardiac abnormalities demonstrated.

The following day the aortic valve was explored. Large tears were found in the non coronary and left coronary cusps. The non coronary cusp was torn from commissure to commissure along the base and the left coronary cusp in similar fashion along the cusp margin as shown in Fig. 2. The valve tissue otherwise appeared normal. Since tears of this type in an otherwise normal valve are not amenable to plastic repair, the valve was excised and replaced with a #9 Starr-Edwards ball valve prosthesis.

Fig. 1. Pre-operative

His post-operative convalescence was free of complications. On the 13th post-operative day, the fractured right femur was treated with intramedullary nailing without incident. Partial weight bearing was begun on the 30th hospital day and on the 42nd hospital day he was discharged with arrangements made for appropriate follow-up examination. Prior to discharge, several carious teeth fractured during the accident were extracted. Appropriate antibiotic coverage was given. He was last examined by us on 1/30/68. At that time the patient was doing quite well, being maintained on long term anticoagulant therapy. He subsequently moved out of state; however, follow-up contact four years later revealed no important sequela from his accident or therapy.

DISCUSSION

Traumatic aortic regurgitation is a rare lesion and occurs almost exclusively in males.[4] It can be secondary to unusual strenuous effort or direct trauma. It is thought that injury occurs when the ventricles are in early diastole and the aortic valves therefore under normal maximum

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tension. The ruptured valve is generally the seat of preceding pathology such as bacterial endocarditis, rheumatic valvitis, syphilis, atheromatous degeneration or congenital anomalies.[8,9] Rarely the valve is normal as reported in this case. Frequently the insufficiency is part of an extensive tear involving the root of the aorta.

The first case of traumatic aortic insufficiency was reported in 1830 by Plenderleath.[10] In 1928, Howard[11] collected 113 cases of traumatic valvar disease from the literature most of which were unproven. Forty-seven cases were due to trauma and of this group only 14 were proven by autopsy. Additional cases were reported in 1936 by Kissane[12] and in 1947 by Bushong.[9] In 1951, Carroll[13] stated that emphasis must be placed on prevention of the underlying rheumatic and syphilitic heart disease since little could be done for these patients once a rupture of the valve had occurred. As late as 1953, Bean and Schmidt[11] questioned the value of discovering rupture of the aortic valve during life since there was no adequate therapy available.

The mean duration of life after trauma producing aortic insufficiency in patients who survive the immediate effect is reported to be approximately 40 months. The prognosis in these patients is of course variable depending upon the degree of valve destruction, the patient's age and their general well-being.

Successful partial physiologic correction of traumatic aortic valve rupture was first accomplished in 1955 by Hufnagel using his valve in the descending aorta.[8] In 1964, the first successful report was made of complete surgical correction of traumatic aortic insufficiency by Beall and Shirkey.[15] Their patient was a 41-year-old woman also involved in an auto accident who underwent initial surgery in November of 1961 at which time a plastic repair was done. Over the subsequent 20 months, progressive cardiac decompensation resulted in re-exploration and successful replacement of the damaged valve.

Conclusion

Traumatic aortic valve insufficiency is a rare lesion and may occur with only minimal external or radiological evidence of chest trauma. The importance of recognizing this lesion is stressed since without appropriate therapy the prognosis is poor. Present day surgical intervention carries a very low risk and affords significant palliation.

Summary

A case of traumatic aortic valve insufficiency occurring in a normal valve has been reported. The case illustrates the rarity of this lesion, the degree of intrathoracic injury which can occur with only minimal external evidence of trauma, and the importance of early recognition of the lesion and institution of appropriate therapy.

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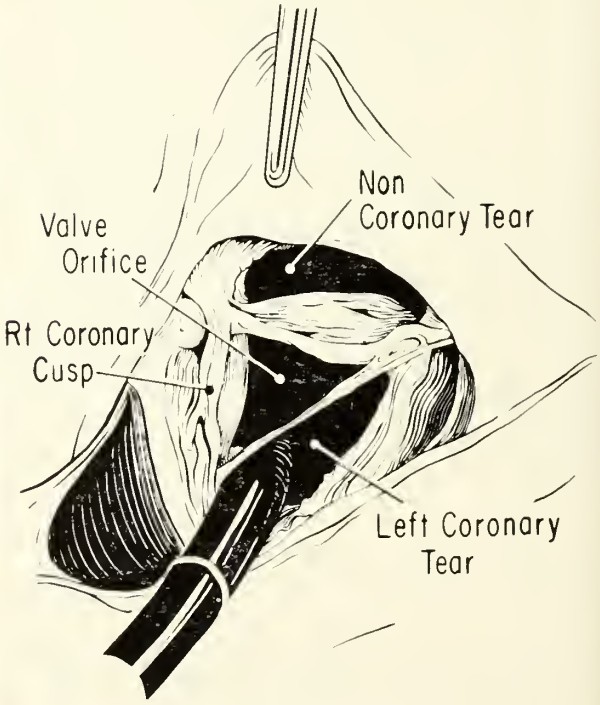

Fig. 2. Operative findings

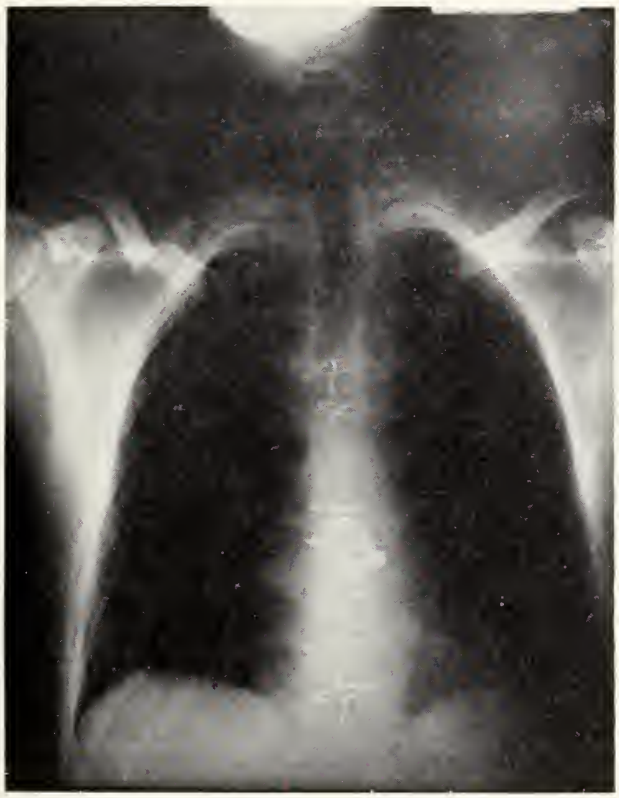

Fig. 3. Post-operative

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CONSUMPTION COAGULOPATHY ASSOCIATED WITH ABDOMINAL AORTIC ANEURYSM

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Acknowledgement

We wish to thank Patricia Baldwin, R.M.T., for the assay studies of FSP.

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Encephalopathy With Fatty Degeneration of the Liver (Reyes Syndrome)

Report of Four Cases In Maine

George W. Hallett, M.D.*

In 1963, R.D.K. Reye[1] of Australia reported a series of 21 bizarre cases of encephalopathy, accompanied by fatty degeneration of the liver, kidneys, and, in some cases, the pancreas. These first reports were followed in subsequent years by similar ones from the United States,[2] New Zealand,[4] and other areas of the United Kingdom. Reye's original cases were all children between the ages of 5 months and 8 years, of which two-thirds were female. Characteristically, the disease started off with a mild respiratory infection, followed by the abrupt onset of rather severe vomiting, and then a rapid progression to wild delerium, seizures, stupor, coma, and death. The majority of the children had hepatomegaly, respiratory rhythm abnormalities, and hypertonic extremities. Many cases had hypoglycemia and low cerebrospinal sugar, and all tested cases had elevations of SGOT, SGPT, Prothrombin Time, and BUN. Seventeen children died, all within two and one-half days of onset. At autopsy, all cases revealed a bright yellow liver, which on microscopic section showed fatty infiltration of parenchymal cells, and absence of necrosis or inflammation. Similar findings were present in renal proximal convoluted tubules, and in the loops of Henle. The brain was always grossly swollen, as were the astrocytes and oligodendroglia. As in the liver, neither kidney nor brain showed evidence of inflammation.

In the past year, four cases closely approximating these patterns have been seen at the Maine Medical Center.

Case Reports

Case I. A female, age 6 years, was admitted on 5/28/69. This patient's past history was essentially normal. She had been well until three days prior to admission, when she complained of intermittent abdominal pain. The following day, mild fever developed, pain continued, accompanied by frequent, severe vomiting, which persisted until the day before admission. On the day of admission, the patient acted "out of her mind," threw objects about randomly, and then lapsed into a coma. She had been admitted to another hospital where she had received 10 mgm of Compazine® I.M., and 5 mgm by rectum. Because of deepening coma, she was transferred to the Maine Medical Center.

Physical examination on arrival showed a 6-year-old semi-stuporous girl, with dilated but reactive pupils, and responding slightly to pain stimuli. Her fundi were normal, as were Dollseye movements, gag reflex, and deep tendon reflexes. Babinski's were positive bilaterally. There was slight tenderness at the right costal margin, but no liver enlargement. Laboratory studies (see Table I) showed marked elevations in liver enzymes, uric acid, blood ammonia, slight elevation of bilirubin, and increased prothrombin time. Treatment consisted of 5% glucose in ¼N saline, and Aquamephyton.® The day after admission the patient had normal pupils and was out of coma. Two days later she was alert and eating well, and four days after admission all studies had returned to normal. She was discharged in seemingly good health. Her case was subsequently presented to Dr. Sydney Gellis of Tufts University Medical School, who agreed that she was a case of Reyes Syndrome, with recovery.

Case II. J.C., a 4-year-old male, was admitted to the Maine Medical Center on 6/30/69. He had been well prior to admission except for a known mild pulmonary valvar stenosis. The morning of admission, he had overslept, woke up, eaten breakfast, and promptly vomited. He went back to sleep for a few minutes, but then awoke again in an agitated, incoherent state and ran around with his hands held high in the air "shrieking like a wild thing." Vomiting persisted, he lost recognition of his family, and quickly lapsed into a stuporous state. Seizures then developed, with doubling at the waist, and rigidity of the extremities. He was admitted to a local hospital, but after several uncontrollable seizures, was transferred to the Maine Medical Center.

Physical examination showed a thin, small 4-year-old male with relaxed expression and closed eyes. There was no elevation of temperature, and vital signs were unremarkable. Pupils were equal and reactive, fundi were normal, and Dollseye movements intact. There were no abnormal reflexes, and the neck was supple. A Grade III systolic murmur was present, loudest in the second left intercostal space. The liver was not enlarged. Laboratory studies, (summarized in Table I), showed slight elevation of bilirubin, liver enzymes and a marked rise in uric acid. Blood sugar was 25 mgm% (checked twice), and CSF sugar was 15 mgm%. The patient was given 25cc of 50% glucose, woke immediately, and was able to recognize his parents. Glucose tolerance test on the day after admission showed a fasting sugar of 72 mgm%, followed by levels at 1, 2, and 3 hours of 140 mgm%, 104 mgm%, and 121 mgm%, respectively. BUN, Glucose, Uric Acid, Bilirubin, and SGOT returned to normal levels 3 days after admission, and the patient was discharged on the fourth hospital day in apparent good health.

Case III. G.J., a 2½-year-old male, had a positive past medical history in that he had been slow in development and had undergone three or four seizures before reaching a year of age. Neurological workup had shown no specific abnormalities, and the patient had been placed on maintenance doses of Dilantin® and Phenobarbital. He had been quite well until 2/11/70, when he suddenly developed a prolonged one hour seizure. He was rushed to a local hospital, where I.V. Amytal® was administered, stopping the convulsive movements. However, vomiting occurred several times, fever developed, and the patient became unresponsive. Two lumbar punctures were negative. After four days of hospitalization, the patient was transferred to the Maine Medical Center.

Physical examination showed a fairly well developed male who unresponsive to all stimuli except pain. Both pupils were widely dilated, and there was no light reflex. Fundi were nor-

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Contraindications—Acute renal insufficiency, rapidly progressing impairment of renal function, anuria and hyperkalemia.

Warnings—Potassium supplementation may cause hyperkalemia and is not indicated unless a glucocorticoid is also given. Discontinue potassium supplementation if hyperkalemia develops.

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Precautions—Patients should be checked carefully since electrolyte imbalance may occur. Although usually insignificant, hyperkalemia may be serious when renal impairment exists; deaths have occurred. Hyponatremia, manifested by dryness of the mouth, thirst, lethargy and drowsiness, together with a low serum sodium may be caused or aggravated, especially when Aldactone is combined with other diuretics. Elevation of BUN may occur, especially when pretreatment hyperazotemia exists. Mild acidosis may occur. Reduce the dosage of other antihypertensive drugs, particularly the ganglionic blocking agents, by at least 50 per cent when adding Aldactone since it may potentiate their action.

Adverse Reactions—Drowsiness, lethargy, headache, diarrhea and other gastrointestinal symptoms, maculopapular or erythematous cutaneous eruptions, urticaria, mental confusion, drug fever, ataxia, gynecomastia, mild androgenic effects, including hirsutism, irregular menses and deepening voice. Adverse reactions are infrequent and usually reversible.

Dosage and Administration—For essential hypertension in adults the daily dosage is 50 to 100 mg. in divided doses. Aldactone may be combined with a thiazide diuretic if necessary. Continue treatment for two weeks or longer since an adequate response may not occur sooner. Adjust subsequent dosage according to response of patient.

For edema, ascites or effusions in adults initial daily dosage is 100 mg. in divided doses. Continue medication for at least five days to determine diuretic response; add a thiazide or organic mercurial if adequate diuretic response has not occurred. Aldactone dosage should not be changed when other therapy is added. A daily dosage of Aldactone considerably greater than 75 mg. may be given if necessary.

A glucocorticoid, such as 15 to 20 mg. of prednisone daily, may be desirable for patients with extremely resistant edema which does not respond adequately to Aldactone and a conventional diuretic. Observe the usual precautions applicable to glucocorticoid therapy; supplemental potassium will usually be necessary. Such patients frequently have an associated hyponatremia—restriction of fluid intake to 1 liter per day or administration of mannitol or urea may be necessary (these measures are contraindicated in patients with uremia or severely impaired renal function). Mannital is contraindicated in patients with congestive heart failure, and urea is contraindicated with a history or signs of hepatic coma unless the patient is receiving antibiotics orally to "sterilize" the gastrointestinal tract.

Glucocorticoids should probably be given first to patients with nephrosis since Aldactone, although useful for diuresis, will not directly affect the basic pathalagic process.

For children the daily dosage should provide 1.5 mg. of Aldactone per paund of body weight.

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Contraindications: Glaucoma, urinary bladder neck or pyloric obstruction, duodenal obstruction and cardiospasm. Hypersensitivity to any of the ingredients.

Warning: Do not exceed recommended dosages.

Precautions: Administer with caution to persons with known idiosyncrasy to atropine and cardiac disease. While under this therapy the urine is blue; patients should be so advised to allay apprehension.

Adverse Reactions: Neither irritation nor untoward reactions have been reported; however, if pronounced dryness of the mouth, flushing, or difficulty in initiating micturition occurs, decrease dosage. If rapid pulse, dizziness or blurring of vision occurs, discontinue use immediately. Acute urinary retention may be precipitated in prostatic hypertrophy.

Dosage and Administration: Adults: Two tablets, orally, four times per day, followed by liberal fluid intake. Older children reduce dosage in proportion to age and weight.

How Supplied: Bottles of 50, 500 and 1,000 tablets.

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TABLE 1

SMA 12/60 AUTOTECHNICON

	Patient D.L.		Patient J.C.		Patient G.J.		Patient T.B.	
	5/29/69	6/2/69	6/30/69	7/3/69	2/11/70	2/16/70	6/1/70	
Wbc	9,000		8,180		26,600		16,200	
Urine albumin	0	0	0	0	3+	0	1+	
Urine Cells	Rbc 10-15	Rbc 0-1	0	0	2-4 Rbc 6-8 Wbc	15-25 Rbc 30-40 Wbc	2-4 Wbc	
CSF Protein	18 mg%	18	65	Not Done	17	Not Done	Not Done	
CSF Glucose	107 mg%	107	15	Not Done	71	Not Done	Not Done	
Blood Glucose	135 mg%	80	25	92	106	85	43	
BUN	34 mg%	12	26	10	13	8.0	29	
Calcium	9.4 mg%	9.8	10.2	10.5	7.8	8.2	7.3	
Phosphorus	4.8 mg%	4.4	3.8	4.7	3.7	4.3	2.6	
Prothrombin Time	22% sec	74%	87%	Not Done	18%	87%	Not Done	
Bilirubin	1.0 mg%	0.4	1.5	0.3	2.1	0.9	1.6	
Ammonia	220 mcg%	60	Not Done		98	129	1740	Normal=18-48 mcg%
Alk. Phosph.	230 mU/ml	137	158	130	290	182	1.25	Normal=30-85 mU/ml
LDH	780 mU/ml	160	210	210	1220	950	900	Normal=90-200 mU/ml
SGOT	480 mU/ml	74	195	50	2680	420	1090	Normal=10-50 mU/ml
Uric Acid	9.5 mg%	2.0	9.6	1.8	7.5	5.7	10.5	Normal=2.5-8.0 mgm%
EEG	Not Done		Very Abnormal		Very Abnormal		Not Done	

mal, and there were no Dollseye movements. DTR's were active, but there were no abdominal reflexes, no grasp or sucking reflexes, and Babinski's were positive. The liver was not palpable. Laboratory studies (Table I) showed markedly increased liver enzymes, uric acid and blood ammonia, and slightly increased bilirubin. Prothrombin time was reduced to 18%. There was no hypoglycemia at either hospital.

This patient had deteriorated markedly from his usual developmental state, and the deterioration continued. Over the next few weeks, he became very unresponsive, failed to recognize his family, and subsisted only by nasogastric tube feeding. Brain scan was normal, and EEG showed changes consistent with mild brain atrophy. Liver enzyme studies returned to normal very slowly over a 6-week period. At the time of discharge, he was functioning at the level of a three-month infant, and appeared permanently and severely brain damaged.

Case IV. T.B., a 3-year-old female, was admitted to the Maine Medical Center 5/31/70. She had been well until 1 week before, at which time she developed a runny nose. One day prior to admission, she awoke with vomiting, followed all day by drowsiness, waking only to vomit. An "alcohol smell" to her breath was noted by parents. Twelve hours later, she seemed drowsy and very thirsty, but she continued to be rational. A few hours later she became unresponsive, temperature rose to 102°, and a generalized seizure developed. She was taken to a local hospital, where an L.P. was performed which was normal, as were serum electrolytes. Blood sugar was 55 mgm%. Her condition worsened rapidly, and she was transferred to the Maine Medical Center.

Physical examination at the time of admission showed an unresponsive 3-year-old female, temperature 103°, responsive only to pain, with weak gag and corneal reflexes. Skin color was sallow, respirations and pulse were irregular, and there were occasional twitchings of all extremities. X-rays of skull, chest, and abdomen were normal, as were serum electrolytes except for a CO_2 content of 16 volumes %. BUN was 17 mgm%, blood glucose was 43 mgm%, and liver enzymes, uric acid, and blood ammonia were markedly elevated (Table I). I.V. glucose was administered, but six hours after admission the patient became suddenly and totally unreactive, pupils became unequal, and she went into cardiopulmonary arrest. She was resuscitated immediately, intubated, and placed on an MA-1 respirator, but temperature, pulse, and blood pressure dropped, and she was pronounced dead about 12 hours later. Permission for autopsy was granted.

Postmortem findings:

Liver: Grossly, diffuse light yellow color, the usual liver markings obscured by yellow fatty infiltration. Microscopically, diffuse swelling of parenchymal cells was present, with granular and frequently finely vacuolated cytoplasm. Fat stains showed variable degrees of staining, with small granules irregularly distributed.

Kidneys: Grossly, not remarkable. Microscopically, albuminous degeneration of the epithelium of the convoluted tubules, particularly the proximal convoluted tubules was evident. Fat stains of the kidney were negative for the most part, except for a few very fine globules in the proximal convoluted tubules.

Brain: Grossly, slight edema and congestion. Microscopically, a mild patchy neuronal loss was noted, along with slight loss of Purkinje cells in the cerebellar cortex.

Other organs: No essential abnormalities on either gross or microscopic.

COMMENT

Although the four cases presented have many similarities, the diagnosis of Reyes Syndrome can only be documented in the single patient who died. However, although Reyes reported survival in only 4 of his 21 cases, subsequent authors[5] have felt that the disease probably occurs in mild form, with frequent survival.

Speculation as to etiology has revolved mainly around toxins and viral agents. In none of our cases was there any history of poison ingestion, and, when performed, serum barbituate, salicylate, and bromide levels were normal, as was urinary ALA. Serum electrolytes, carried out

in every case, were entirely within normal limits. Reyes had pointed out similarities between his syndrome and the "Vomiting Sickness of Jamica," a disease supposedly due to the ingestion of a toxic herb present in bush tea. This disease has a similar course ro Reye's Syndrome, occurs only in children under 10 years of age, and, at autopsy, is also characterized by fatty changes in the liver and kidneys. In addition, however, there are widespread necroses of parenchymal cells, which are at marked variance with Reyes cases.

Subsequent to the original report, similar children have been described all over the world. Almost all cases show vomiting, irrational behavior, and liver enzyme changes – but some series report hypoglycemia in only one out of four cases.[3] In two New Zealand children, survival occurred with permanent brain damage.[4] Huttenlocker reported 10 patients collected over a 5-year period ending in 1969, in which extensive viral studies were negative. Feeling that many of rhe cerebral symptoms mighr be attributed to ammonia intoxication, he attempted exchange transfusions on three cases, but all died. Three out of four other children, who received nothing bur glucose, survived, although one had irreversible brain damage. In May 1970, Pross, Bradford, and Krueger reported a case treated by peritoneal dialysis. Their rationale was that ammonia should theoretically combine with hydrogen ion to form the dialyzable ammonium ion, and that such rherapy would also benefit acidosis and hypoglycemia. Their one case developed a rapid decrease in ammonia levels and survived. It should be noted, however, that this patient had an initial salicylate level of 25 mgm/100ml.

SUMMARY

Four children with combined encephalopathy and liver enzyme elevations are presented. These cases appear to fit into the clinical and laboratory patterns first described by Reyes as "Encephalopathy with Fatty Degeneration of the Liver," and later shortened to the easier term "Reyes Syndrome." Two children survived without residual, one suffered permanent brain damage, and one died. Autopsy on this case confirmed the clinical diagnosis; Australian (Hepatitis) antigen was tested for in this case, and found to be negative. Of interest in these four cases, and not previously reported, were initial high uric levels with rapid falls to low normal upon recovery.

It would seem that Reyes Syndrome should be seriously considered in the differential diagnosis of coma in the pediatric age group. To paraphrase our British friends:

"The Reyes in Maine
Are Plainly here to Reign"

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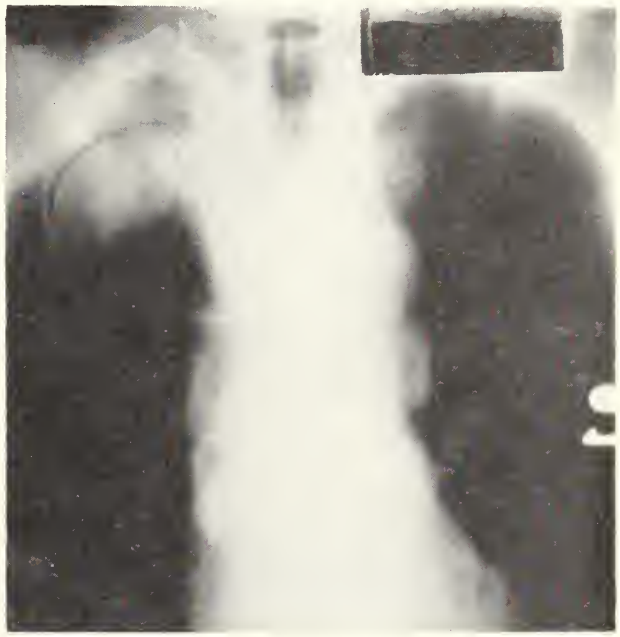
Contact Francis J. O'Connor, M.D., Tel. 623-4711 (Augusta General Hospital), or Mr. Norman Powers, R.T., course coordinator.

X-Ray Of The Month*

Clinical Summary

This 55-year-old man was seen because of a chronic productive cough. A conventional chest film showed a lesion in the right upper lobe, and tomography showed the presence of an oval density within a cystic structure at the right apex.



Diagnosis: Pulmonary Intracavitary Fungus Ball

The findings of the rounded mass within a thin-walled cavity in the apical region of a lung with a crescent of air between the mass and the cavity wall are virtually pathognomonic for this condition.

The essential feature of pulmonary intracavitary fungus ball is a mass of mycelia of Aspergillus or Candida lying within a pulmonary cavity communicating with the bronchial tree.

These patients frequently, but not invariably, present with hemoptysis. They are otherwise in excellent health without fever, pain or weight loss. When hemoptysis is not present, a productive cough frequently is. Laboratory studies are characteristically negative, including work-up for tuberculosis.

The lesion is almost always found in the upper lobes and rarely in the superior segment of a lower lobe. Another important characteristic in the diagnosis is the mobility of the fungus ball within the cavity as determined fluoroscopically. The lesion is remarkably stable when followed over a long period of time.

The pathogenesis is thought to be fortuitous invasion of a pre-existing pathological area of the lung as a cyst or a pneumatocele by saprophytic species of Aspergillus or Candida.

The differential radiological diagnosis includes pulmonary hydatidosis which occasionally will simulate a fungus ball; however, this lesion tends not to be stable. At times an inspissated blood clot in an abscess cavity can have this appearance.

*From the Department of Radiology, Maine Medical Center, Portland, Maine 04102.

Reference

Emanuel J. Levin, Pulmonary Intracavitary Fungus Ball, Radiology, Volume 66, Page 9, January 1956.

Report of A.M.A. Delegate

George W. Wood, III, M.D.

The American Medical Association House of Delegates held its annual meeting in Chicago from June 21 to June 25th, 1970. They considered 201 reports, resolutions, and other items of business and watched and participated in "politicking" for various elected officers of the Association.

From the many issues discussed, I have selected a very limited number to report specifically on, but would welcome any questions regarding other items the M.M.A. Council would be concerned with.

1. Consumers' Forum.

Sunday afternoon of the 21st the committee headed by Dr. Malcolm Todd of California listened for 3 and one-half hours to various consumers. You, I am sure, have read about the discussion in the *A.M.A. News,* and other media. This observer felt that the committee did a good job and such meetings should be held with each session of the A.M.A. House of Delegates. We do need more direct contact with various attitudes outside the profession.

2. Abortion.

This was discussed heatedly. The following statement was adopted:

> "Whereas, abortion, like any other medical procedure, should not be performed when contrary to the best interests of the patient since good medical practice requires due consideration for the patient's welfare and not mere acquiescence to the patient's demands; and
> "Whereas, the standards of sound clinical judgement, which, with informed patient consent should be determinative according to the merits of each individual case; therefore be it
> "Resolved, that abortion is a medical procedure and should be performed only by a duly licensed physician and surgeon in an accredited hospital acting only in conformance with standards of good medical practice, and after consultation with two other physicians chosen because of their professional competence, and within the medical practice act of his state; and be it further
> "Resolved, that no physician or other professional personnel shall be compelled to perform any act which violates his good medical judgement. Neither physician, hospital, nor hospital personnel shall be required to perform any act violative of personally held moral principles. The circumstances, good medical practice requires only that the physician or other professional personnel withdraw from the case so long as the withdrawal is consistent with good medical practice."

3. Dues.

This seemed like old times to your A.M.A. delegate. I will not re-hash all aspects of this problem but will say that three points were clearly made: a) The House of Delegates changed the bylaws so that the dues will be set by the House of Delegates rather than the Board of Trustees; b) That the dues, instead of being increased $80.00, will be increased $40.00; c) It is incumbent upon the A.M.A. and the state societies to inform all physicians of the reasons for this increase and plans for the future.

4. Committee on Long Range Planning & Development.

The multiple recommendations were discussed by varying reference committees. Your delegate had forwarded resolutions regarding selected recommendations. It is my opinion that for the most part the A.M.A. House of Delegates responded positively to this progressive report although there were some changes which he could not agree with.

5. Professional Liability.

The A.M.A. is moving rapidly forward in this area of developing a program which would be a combination of A.M.A. and state society responsibility.

6. Peer Review.

This received re-emphasis and really has met no significant resistance in any discussion.

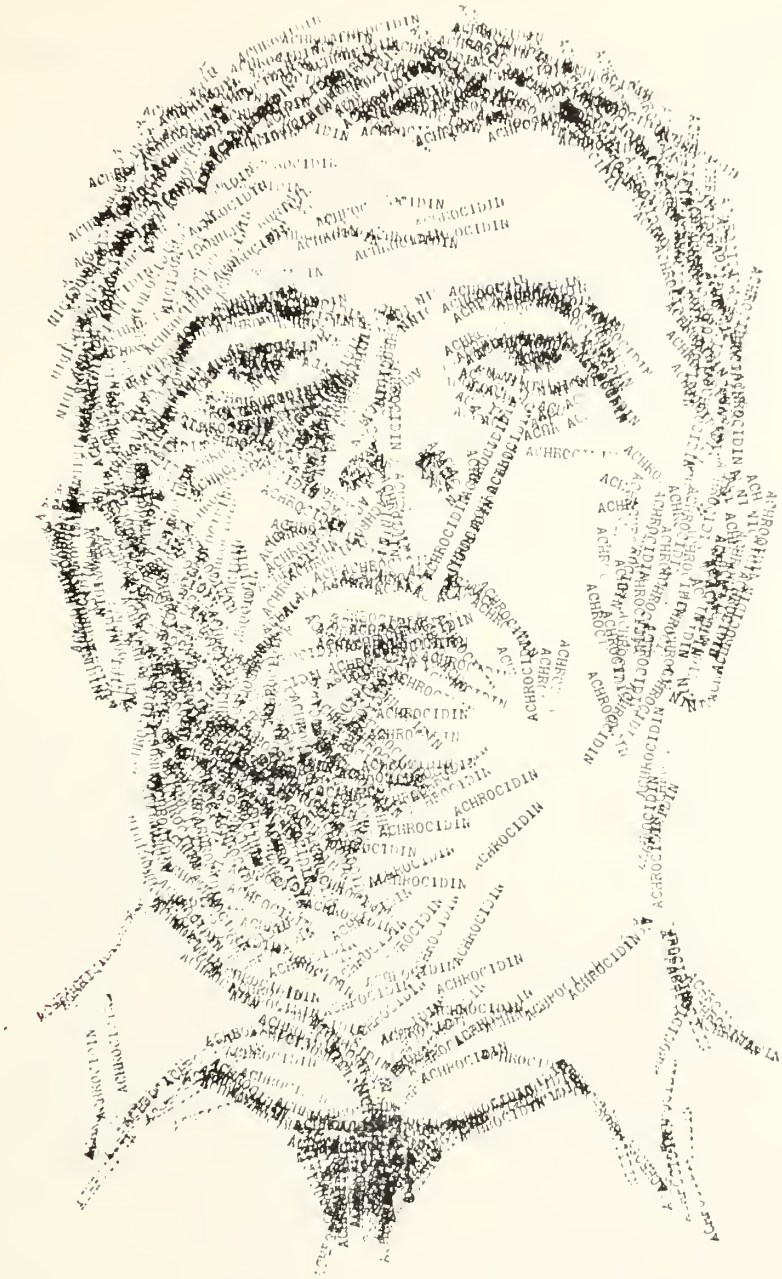
7. Universal Health Insurance.

The medi-credit program of A.M.A. was discussed, and will continue to be effectively presented to the Congress.

Thus, you see above some of the major issues before us. We toward the last turned our concern toward the men who might best expound on these issues. There were six candidates running for four Trustee offices. For the most part, a generally conservative group won in each instance, but at least in two instances, although the men tend to be in this direction, I think they are very sound individuals. The 4-way race for the President-elect came down to the wire with Dr. Long against Dr. Hall. The majority of the New England delegation I think supported Dr. Long, but, as you know, he lost.

From all of this debate and politicking, what might one assume? I have the continued strong feeling that the A.M.A. has changed its attitude and direction over the last three to five years and am quite encouraged by its progress. It is interesting to note that the press generally gave it somewhat more favorable coverage than usual. Whether this is good or bad might be debated by some.

Dr. Richard P. Laney and your president Charles R. Glassmire, M.D., were very effective supporters of the Maine Medical Association in their contacts at the A.M.A. It was a great pleasure to work with them.



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535-9

DEAN H. FISHER, M.D.
COMMISSIONER

State Of Maine

Department of Health and Welfare

Department of Health and Welfare
Division of Eye Care and Special Services
An Evaluation of the Armed Forces Rejectee Program*

The Services to Armed Forces Rejectees, a component of the Division of Eye Care and Special Services, Maine Department of Health and Welfare, became operational in 1965. It was known that 32% of those young men in Maine called up for pre-induction physicals were found disqualified for medical reasons.** This constituted the third highest percentage of medical disqualifications in the country. It was further known that while Maine's figure of acceptability of young men who took both induction and pre-induction examinations was .5% higher than the national average, at the same time the 34.5% disqualified for medical reasons was 6% higher than the national average. Rejections for administrative and mental reasons were lower in Maine than in many states. Maine has the seventh highest percentage (92.6%) in the nation of young men passing their final induction physical which is a testimony to the thoroughness and competence of the pre-induction physical activity.

A procedure of interviewing all physical and psychiatric rejectees by SAFR counselors was begun at the Bangor Armed Forces Entrance and Examining Station in September 1965, and at a similar facility in Portland in November of the same year. The objective of the program as stated in the original grant request was to provide rejectees with counseling, referral to health resources, and follow-up "to help make them more productive members of society." Unfortunately, at no time during the existence of the project was the program outlined within the framework of "objectives," "sub-objectives," and "activities" as we now know them to be important, particularly in evaluating program effectiveness. Consequently, in designing an evaluation of this program early in 1969, it became difficult to set up specific measures of accomplishment of sub-objectives which had not been clearly defined.

In retrospect, one could say the objective of the program in all probability should have been "to reduce in Maine the social and economic impact resulting from psychiatric and physical disabilities of Armed Forces medical rejectees." The rejection each year of nearly 2,000 young men in Maine for military service because of psychiatric or physical disability may constitute an identifiable and researchable universe to provide some clues for the causes of disability and methods of reducing disability.

Sub-objectives could have been:

1. To identify reasons for rejection;
2. To establish the impact of the cause for rejection on social and economic productivity or rejectees;
3. To identify resources that exist to lessen the impact of the disability including:
   a. medical
   b. social
   c. educational
   d. vocational

   and identify problems (if any) in the utilization of these resources;
4. To establish if and how maximum utilization can lessen the economic and social impact;
5. To identify methods of more effectively utilizing resources;
6. To identify gaps in resources and recommend ways in which gaps can be minimized; and
7. To act as the catalyst for development of more adequate resources and establish patterns for the most effective utilization of them.

But these were not stated "objectives" or "sub-objectives." The program was designed within the framework of U. S. Public Health Service guidelines:

> "Implement a system of evaluating medical needs of rejectees; counsel young men on their needs; refer them to appropriate private or public health resources; and take the necessary

*This report reflects activities funded through Section 314 (d) of PL 89-749 for the period from January 1, 1969 to March 31, 1969.

**Supplement to *Health of the Army,* Results Of The Examination of Youths for Military Service, March, 1967, Office of the Surgeon General.

follow-up action to assure that those needing medical care are getting it."

Appropriately, in December of 1968, came the question: What is this program accomplishing? Further questions were posed: What are the major kinds of disabilities of all Armed Forces rejectees in Maine? Has utilization of medical and other community resources been productive for the rejectees? Has employability of rejectees been improved? How does the cost of the program stack up against the benefits which accrue to the rejectee and society? Should the program be continued? in its existing form? or with drastic revision?

This document hopefully answers the above questions.

The Program

The Services to Armed Forces Rejectees Program was in existence from the previously mentioned September 1965 until December 1968. Negotiations with the commanding officers, Armed Forces Examining and Entrance Stations resulted in forwarding of medical rejectees to SAFR personnel. A counselor, John D. Dow, worked through the Portland AFEES to interview, counsel, and refer rejectees from York, Oxford, Sagadahoc, Cumberland, Lincoln, Kennebec, Androscoggin, and Franklin counties. Another counselor, John Hoctor, functioned through the Bangor AFEES to serve those rejectees from Waldo, Knox, Penobscot, Washington, Aroostook, Piscataquis, Hancock, and Somerset counties. In 75% of the cases, SAFR personnel were provided with a room to conduct interviews in privacy and possible counseling and or referral activities. Each counselor was provided with a secretary through the SAFR program, one of whom was shared with the State Program Director, whose chief responsibilities included liaison with the military and medical communities, acting as resource coordinator, and interpreter of the program to the public and official agencies. Liaison officials from both the Maine Medical Association and the Maine Osteopathic Association were available for consultation by the SAFR personnel. Annual program costs were approximately $50,000.

From September 1965 through December 1968, the Armed Forces Examining Centers referred 4,700 rejectees to the program; this represented 4,378 rejected for physical reasons, 241 for psychiatric reasons, and 81 rejected for a combination of both.

Of these rejectees, 1,737 were determined to be under adequate medical care and not in need of counseling or referral to other community agencies.

Another 1,859 rejectees did not receive direct referral services from the program for several reasons including refusal of any services, no services required, moving without leaving forwarding addresses, obtaining care through their own initiative, etc.

Referrals of 1,104 rejectees to private and non-private resources were effected by the program staff. These referrals included 865 to private physicians, dentists, etc; 840 were referred for physical defects; 15 for psychiatric problems; and 10 for a combination of both.

There were 239 referrals to a variety of non-private community resources; of these rejectees, 200 had physical defects, 25 had psychiatric disorders, and 14 had a combination of both.

The Evaluation

The basic objective of the evaluation was to determine the effectiveness of the program in alleviating the physical and psychiatric causes of rejection to the extent that the employability of the rejectees was improved.

An evaluation process was designed and the necessary materials were prepared in January 1969. The evaluation was to cover activities pertaining to those 1,682 men rejected at the AFEES and interviewed by SAFR counselors between July 1, 1967 and June 30, 1968. We were interested in the productivity of receipt of health and/or vocational services and the effect of counseling, referral, and receipt of services on employability. We were interested in any possible "non-productive" areas of program activity as they might affect recommendations for future planning. In two months, data was compiled on all rejected during the Fiscal Year 1968.

Of 1,682 rejectees, only 1,612 were included in the sample for the evaluation. The seventy rejectees eliminated from the sample include those who left the State (perhaps to be followed by another Health Referral Service unit), contact failure resulting after the rejectee has been examined and/or interviewed at the AFEES, cases where no defect was subsequently determined to exist, and rejectees who were turned down at least twice within the same fiscal year but who were carried on SAFR rosters more than once.

There were more nineteen-year-olds rejected than any other age group. The largest number of examinations given at the AFEES are so-called "pre-induction" physicals of 18-and 19-year-olds to determine their acceptability for military service. Age breakdown of the rejectees is as follows:

age 17	age 18	age 19	age 20	age 21
8	136	619	310	156
age 22	age 23	age 24	age 25	age 26
110	140	84	49	1

The rejectees came from Maine's sixteen counties (at least, they could give addresses from those counties. It should be noted that college students, seasonal employees, etc., were liberally sprinkled throughout the mix.) Geographical distribution of rejectees was as follows:

County	*Rejectees*	*County*	*Rejectees*
Androscoggin	109	Oxford	107
Aroostook	199	Penobscot	215
Cumberland	327	Piscataquis	20
Franklin	30	Sagadahoc	24

Hancock	59	Somerset	53
Kennebec	156	Waldo	37
Knox	27	Washington	43
Lincoln	47	York	159

The AFEES do not release any breakdown on total examinations that could be compared with the above figures to determine if various geographic areas had higher percentages of rejectees than others.

Causes for rejection covered a broad spectrum. The most frequent cause for rejection was obesity. Three hundred and eleven of 1,612 young men rejected in Maine during the 1968 fiscal year were classified overweight according to military standards. Other causes for rejection and their frequencies included:

Hypertension	292
Eye diseases and defects	246
Functional disease of heart; heart murmur	148
Impaired hearing	131

The general categories of defects and their frequencies among the 1,612 rejectees are as follows:

Infectious and parasitic diseases	4
Neoplasms	66
Allergic, metabolic, endocrine, and nutritional diseases	471
Diseases of blood and blood-forming organs	8
Psychoses, psychoneurotic, and personality disorders, etc.	116
Diseases of the nervous system	36
Eye diseases and defects	256
Diseases of ear and mastoid process	171
Diseases of the circulatory system	468
Diseases of the respiratory system	9
Diseases of the digestive system	159
Diseases of the genito-urinary system	120
Diseases of the skin	53
Diseases of bones and organs of movement	320
Congenital malformations	12
Miscellaneous	38

One thousand four hundred and thirty-two rejectees were aware of the existence of the defects for which they were rejected, while 180 were not.

Two hundred and thirteen rejectees were unemployed at the time of rejection. Another 213 rejectees were either high school, vocational school, or college students. Occupations ranged from accountants to writers with the largest specific grouping being that of "laborer."

Defects affected employment of 488 rejectees, 45 severely and 443 moderately. In 1,124 cases, defects did not affect employment.

And finally, of the total sample, 818 of the 1,612 were not under medical care at the time of rejection. Those rejectees not under medical care were to become the "target" group which the program was designed to assist.

However, 601 of the 818 members of the "target" group declined the services of the program. This was done sometimes at the initial interview or at subsequent interviews, other times after referral appointments had been made.

Obesity and hypertensive conditions headed the list of defects of the 601 rejectees.

Nevertheless, with 601 declinations, the program was concerned with providing services to 217 young Maine men who had been rejected from the Armed Forces for physical and psychiatric reasons during the 1968 fiscal year.

Let's look at the profile of those 217 who received services. Age breakdown of the rejectees is as follows:

age 17	age 18	age 19	age 20	age 21
3	19	100	38	20
age 22	age 23	age 24	age 25	age 26
5	20	8	4	0

Geographical distribution is as follows:

County	*Rejectees*	*County*	*Rejectees*
Androscoggin	8	Oxford	18
Aroostook	27	Penobscot	37
Cumberland	38	Piscataquis	4
Franklin	0	Sagadahoc	2
Hancock	4	Somerset	12
Kennebec	19	Waldo	4
Knox	5	Washington	8
Lincoln	7	York	24

The most frequent cause for rejection among this group was hypertension, which was reported in 69 cases. Obesity followed having been a cause for rejection in 49 instances. Other causes of rejection and their frequency include:

Impaired hearing	24
Heart murmur	33
Visual defects	29

The general categories of defects and their frequency among the 217 rejectees are as follows:

Infectious and parasitic diseases	0
Neoplasms	9
Allergic, metabolic, endocrine, and nutritional diseases	56
Diseases of blood	0
Psychoses, psychoneurotic, and personality disorders	17
Diseases of the nervous system	1
Eye diseases and defects	35
Diseases of ear and mastoid process	29
Diseases of the circulatory system	107
Diseases of the respiratory system	3
Diseases of the digestive system	13
Diseases of the genito-urinary system	26
Diseases of the skin	1
Diseases of bones and organs of movement	8

Congenital malformations	1
Miscellaneous	5

Of the 217 who received services, 21 were unemployed at the time of rejection and 28 were students. Those employed were engaged in a wide-range of occupations.

What did these 217 receive for medical services?

201 received professional counseling (either medical or psychiatric)
14 underwent surgery
169 received medical treatment
24 received other medical services (physiotherapy, etc.)

What were the results of the receipt of these medical services?

48 rejectees reported improved employability
8 rejectees reported upgrading their employment

Forty-six of the rejectees received vocational guidance counseling, all received vocational training, 3 schooling, and 6 job placements as a result of the program. Improved employability as a result of guidance counseling, training, and/or schooling was reported in 36 cases with an upgrading of employment in 6 instances.

It is interesting to note that 145 rejectees indicated they received medical services they would otherwise not have received, and 21 indicated receiving vocational services which would otherwise not have been received. One hundred and eleven rejectees stated they did not previously know of the availability of medical services they received while 14 made similar comments about vocational services.

Where are the 217 rejectees today (as of March 31, 1969)?

In Armed Services	19
Employed	175
Unemployed	8
In school	15

Limited staff time prevented the gathering of data on the financial impact of the improved employability and upgrading of employment of rejectees receiving services.

Based on the end-product, in all probability the expenditure of $50,000 a year is a reasonable one. The improved employability of rejectees and up-grading of employment should over a period of years pay dividends to society through increased productivity. These dollars should be paid back through increased earning power. But, in the light of the necessity for establishing priorities in spending for health needs, this $50,000 might well be spent more effectively in other ways. The end-products of the Services to Armed Forces program could have been achieved at a significantly lower cost per case. However, the Federal guidelines of the program required certain activities including mass screening, which were not particularly productive in terms of getting young men under care to alleviate physical and psychiatric disorders.

For example, *all* Armed Forces rejectees had to be interviewed at the Armed Forces Examining Stations. While the information on defects for which all young men are rejected in Maine can be useful, the data has not been put to use at either State or Federal levels. The fact that better than 20% of those rejected were turned down because of obesity, a condition which had existed in a majority of cases for more than five years, should alert us to the possibility that this defect, oftentimes with accompanying hypertension, should be of deep concern to health authorities while these young men are in junior high and high schools.

For example, all rejectees who were not receiving medical care at the time of rejection were to receive counseling to be "motivated" to get under care. Some prospective inductees, unhappy with our involvement in Vietnam (and their prospective involvement), have been relieved to be told of their rejection. Motivation to correct defects with this type of rejectee is near to impossible. In many instances, rejectees at the time of interview would reluctantly agree to referral, and then fail to keep a series of appointments with a resource. This has been "expensive" in terms of staff time and effort. The design of the program was to be of maximum service to a maximum number of rejectees. There is little justification for continuing a program in that design. The amount of time and corresponding expense involved in interviewing those under care and counseling those who "weren't interested" is a questionable use of resources.

For example, all rejectees who might have left the AFEES (because of bus departing, etc.) prior to seeing the SAFR counselor had to be visited in their home towns or contacted to come to the office for interview. Again, time and expense involved with rejectees who wanted no part of our services, many of whom were determined to be under care at the time of rejection.

And so, recommendation number one would be that counseling and referral services be made available to those young men desiring it who are not already under care and that these be made available on a self-referral basis to the Bureau of Rehabilitation Services with forms provided by the Bureau, with AFEES personnel being the intermediaries. Two rehabilitation counselors one in each part of the State functioning on a shared time basis could meet the needs of these rejectees. A close liaison between SAFR and AFEES personnel existed for 3½ years. The acceptance of, endorsement of, and cooperation with the SAFR program by AFEES personnel, AFEES commanders, and Colonel Paul Merrick, State Selective Services Director, lead one to believe that negotiations with the AFEES and Selective Services could result in their aiding in the referral process in the suggested manner. In effect, those young men desiring services would find a counselor ready to aid them.

Recommendation number two would be that immediate steps be taken to upgrade school health and physical fitness programs in an effort to combat obesity. The possibility of developing a state-wide physical fitness co-

ordinating program to marshal community resources to meet the needs of the obese should be explored. Lack of adequate resources to which obese people can turn for help – for motivation, guidance, and medical help – is a major problem in Maine.

Recommendation number three, if followed, could eliminate the necessity of establishing at a future date a screening program to identify defects of Armed Forces rejectees. Seventy percent of the causes for rejection have been in existence five years or over. It has been suggested that perhaps through the use of public health nurses working in the schools, mothers could be organized and trained to check for urinary problems, growth, hearing, oral hygiene, and circulatory problems, such as they now do with vision checks. Mothers could alert the school nurse of any variance from the norms and the nurse could further check and inform the family and school physician of those in need of medical care.

Although the determination of acceptability for military service, in terms of the standards set by the military, is a function of the AFEES, considerable numbers (about ten per month in Maine, according to Colonel Paul Merrick of the State Selective Service headquarters) of registrants are screened out by the local boards without being seen at the AFEES. The local boards prescreen registrants whom they judge – in the course of classification and selection – as obviously not medically qualified for military service. While the determinations of medical unfitness may be made solely by the members of the local boards, they are usually initiated by these members and completed only upon the advice of the medical advisor to the local boards. It would appear that those disqualified for "obvious reasons" might well include many who would need and welcome referral to a variety of community resources (although it's possible many of these rejectees are known to private and public resources). It is recommended that a brief study be made of a sample to learn of causes for rejection at the draft board level, degree of significance of disability in terms of employment as well as familiarity and contact with resources by these rejectees. It could be learned if those needing services the most have been by-passed in our recently terminated SAFR program.

In conclusion, the Services to Armed Forces Rejectees program, burdened as it was with record keeping and unwieldy numbers, effectively provided services to 217 Maine young men rejected from the Armed Forces for a wide variety of reasons. Because of the design of the program, it frequently appeared that the time and efforts of program personnel were spent more on records, rather than on the men and their needs. The program may well prove to be worth the expenditure of funds; however, with the importance of establishing priorities for spending health dollars, it is obvious that the same or greater end-products can be obtained at somewhat lower cost with a substantial re-designing of a Services to Armed Forces Rejectees program.

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Contraindication: Hypercalcemia; neoplastic diseases; and fully digitalized patients. Do not use intramuscularly in infants and young children. Before starting therapy, consult complete product literature.

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Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported. Sympathomimetic cardiovascular effects reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others. Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema. Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tablet daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet three times daily, one hour before meals. If desired, an additional tablet may be given in midevening to overcome night hunger. Use in children under 12 years of age is not recommended.

T-006A / 1/70 / U.S. PATENT NO. 3,001,910

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Prescribing Information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions/Adverse Reactions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

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After only one year:

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Injectable
Garamycin®
brand of
gentamicin sulfate
injection

*An estimated 208,000 patients have received GARAMYCIN Injectable to date. The combined population of Bangor, Lewiston, and Portland is 144,500. (Estimated 1969 figures from The New York Times Encyclopedic Almanac 1970.)

See Clinical Considerations section on last page...

Injectable Garamycin®

brand of gentamicin sulfate injection

Schering

ADULT DOSAGE GUIDELINES

See definitive prescribing information in Package Insert.

Patients with Normal Renal Function

Total Daily Dose (administered in two, three, or four divided doses)			
Urinary Tract Infections (due to susceptible strains of gram-negative bacteria)†	Less Severe 0.8-1.2 mg./kg. for 7-10 days	Resistant/ Moderately Severe Larger doses or additional antibacterial therapy should be considered in severe urinary tract infections or in resistant cases involving the renal parenchyma or anatomic anomaly.	Serious/Life-Threatening up to 5 mg./kg.
Other Infections including bacteremia, infected surgical wounds, severe soft tissue infections, and respiratory tract infections (due to susceptible strains of gram-negative bacteria)	3 mg./kg. for 7-10 days		

†Alkalinization of the urine may be a useful therapeutic adjunct.

Patients with Impaired Renal Function

To minimize the risk of ototoxicity in patients with impaired kidney function, only the first dose should be that normally recommended. Each subsequent dose should be half or less of that recommended for patients with normal renal function, depending upon the degree of renal impairment.

In patients with renal failure who are undergoing 14-hour hemodialysis twice weekly, administration of 1 mg./kg. GARAMYCIN Injectable at the end of each dialysis period has been suggested.

Clinical Considerations

Indications: GARAMYCIN Injectable is clinically effective in infections due to susceptible strains of gram-negative bacteria, including *Pseudomonas aeruginosa,* and species of indole-positive and indole-negative *Proteus, Escherichia coli,* and *Klebsiella-Aerobacter.* Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose. If the susceptibility tests indicate that the causative organism is resistant to gentamicin sulfate, other appropriate antibiotic therapy should be instituted.

IN VITRO INHIBITION OF CLINICALLY IMPORTANT BACTERIA BY GENTAMICIN SULFATE (TUBE DILUTION STUDIES)

BACTERIA	No. of Strains Tested	No. of Strains (%) Inhibited by: 4 mcg./cc. or less		8 mcg./cc. or less*		No. of *In Vitro* Studies
Staphylococcus aureus	1,210	1,200	(99%)	1,206	(99%)	11
Pseudomonas aeruginosa	885	771	(87%)	828	(93%)	16
Escherichia coli	836	736	(88%)	779	(93%)	11
Indole-positive and indole-negative *Proteus* species	477	210	(44%)	358	(75%)	12
Klebsiella-Aerobacter species	292	205	(70%)	231	(79%)	10

*Number of strains (%) of gram-negative bacteria inhibited by 10 mcg./cc. or less are as follows: *Pseudomonas aeruginosa,* 828 (93%); *Escherichia coli,* 792 (95%); *Proteus* species, 393 (82%); *Klebsiella-Aerobacter* species, 284 (97%). From same studies as above.
Source: Package Insert

This drug should be limited to the treatment of serious infections caused by gram-negative bacteria, particularly *Pseudomonas aeruginosa, Proteus* and other susceptible organisms, with due regard for relative antibiotic toxicity. Therefore, the drug should be considered for use against gram-negative: 1. Bacteremia; 2. Infected surgical wounds; 3. Severe soft tissue infections, including burns complicated by sepsis; 4. Respiratory tract infections; and 5. Selected cases of urinary tract infection.

Contraindications: GARAMYCIN Injectable is contraindicated in individuals with a history of hypersensitivity or toxic reactions to gentamicin.

Warnings: Patients receiving treatment with GARAMYCIN should be under close clinical observation because of the toxicity associated with the use of this drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with preexisting renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with preexisting renal impairment. Kidney function diminished by infection of the upper urinary tract may, however, improve during effective treatment with GARAMYCIN Injectable.

Concurrent administration of potentially ototoxic drugs such as streptomycin and kanamycin or of potentially nephrotoxic drugs such as polymyxin, colistin, and kanamycin with gentamicin sulfate has not been shown to afford any clinical advantages and, moreover may result in additive toxicity. Monitoring of vestibular, cochlear, and renal function will provide guidance for therapy in such cases.

Precautions: In patients with impaired renal function in whom serious infection develops, serum concentrations of the drug may rise, with consequently increased risk of ototoxicity. In these patients or in those in whom recommended dosage or duration of therapy must be exceeded as a life-saving measure, routine studies of kidney function should be performed when possible. These may be supplemented by evaluation of the vestibular and auditory function and measurement of serum concentration of the drug when feasible. Serum concentrations of gentamicin should be maintained below the range of 10-12 mcg./ml. to reduce risk of ototoxicity.

Ordinarily, treatment should not be given for more than 7 to 10 days or be repeated unless required for serious infection not responsive to other agents.

As with other antibiotics, treatment with GARAMYCIN Injectable may occasionally result in overgrowth of nonsensitive organisms. If superinfection occurs, appropriate therapy is indicated.

Safety for use in pregnancy or the potential for fetal ototoxicity or nephrotoxicity have not been established. Studies in pregnant animals have not revealed teratogenic or ototoxic effects in the fetus. GARAMYCIN Injectable should not be used in pregnant patients or in women of childbearing age unless its use is deemed advisable by the physician.

Adverse Reactions: The overall incidence of ototoxicity considered related to treatment with GARAMYCIN Injectable was 2.8 per cent (16 of 565 patients). Contributory factors (two or more factors were relevant to most patients) were as follows: 10 had azotemia, 10 received a total of 1 gram or more of the drug, 7 had recently received other potentially ototoxic antibiotics (streptomycin or kanamycin), and 5 were over 60 years of age. Six also had decreased high-tone hearing acuity, which returned to or toward normal in the 4 patients retested.

Analysis of BUN data indicated that 4 (2%) of 172 patients showed increases in BUN that were probably related to treatment with GARAMYCIN Injectable. Of 20 increases probably or possibly related to treatment, 7 were reversible, 9 occurred in terminal patients, and 4 had no follow-up.

Other adverse reactions associated with treatment were one instance each of urticaria, decreased hematocrit, and reversible depression of granulocytes with normal bone marrow. Other rarely reported and possibly treatment-related adverse reactions were anemia, increased reticulocyte count, rash, purpura, drug fever, hypotension, convulsions, twitching, salivation, nausea, vomiting, increased transaminase activity (SGOT or SGPT), increased serum bilirubin, decreased serum calcium, and joint pain.

Packaging: GARAMYCIN Injectable, 40 mg./cc., 2-cc. multiple-dose vials, for intramuscular administration.

For more complete prescribing details, consult package insert or Physicians' Desk Reference. Schering literature is also available from your Schering Representative or Medical Services Department, Schering Corporation, Union, New Jersey 07083.

AHFS CATEGORY 8:12.28 S-029

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Cardiac Pacing in Acute Myocardial Infarction Complicated by Complete Heart Block

. . . Previously it was estimated that complete atrioventricular block occurred in about 1.5 percent of patients with acute myocardial infarction. More recent data indicate a considerably higher incidence.

It would appear that the incidence of complete heart block in myocardial infarction is from two- to fivefold higher than previously suggested. However, McNally and Benchimol . . . believe the true incidence in acute myocardial infarction is "considerably less than 5 percent."

In an attempt to more accurately appraise the results of pacing and possibly establish guidelines for temporary pacing . . . in cases of acute myocardial infarction complicated by complete heart block, a review of the literature was undertaken.

The mortality rate in 315 patients with complete heart block treated with temporary internal pacing was 46.9 percent. This is about the same mortality rate commonly accepted for patients not treated by cardiac pacing. . . .

The appearance of complete heart block in the course of myocardial infarction adversely affects the mortality rate. . . . The optimum improvement in the mortality rate (with cardiac pacing) when projected nationally represents a possible salvage of 1,200 to 1,600 lives annually. . . . While any improvement is, of course, welcome, it is not of such magnitude that it should make one complacent with present methods of treatment. Nor should the appearance of complete heart block in the course of acute myocardial infarction reflexly call for the insertion of an intracardiac pacemaker when the proper facilities or experienced personnel are not readily available. Most reports of pacemaker-treated cases have come from large cardiac centers . . . with extensive experience in routine cardiac catheterization. The surprisingly low incidence of serious complications of catheterizations . . . in the presence of acute myocardial infarction attests to the skill and judgment of these physicians. Because of the existing widespread enthusiasm for cardiac pacing in complete heart block in the setting of acute infarction, it is possible that the indiscriminate insertion of catheters by inexperienced personnel without proper facilities could adversely affect a precarious situation and reverse the slight balance favoring pacemaker therapy.

A more rational approach . . . is the careful evaluation of each patient . . . to determine whether pacemaker therapy is indicated. Of greatest importance in arriving at a decision are the following: location of the myocardial infarction, ventricular rate, presence or absence of abnormal intraventricular conduction disturbance, appearance of Mobitz Type II block, presence of Stokes-Adams episodes, and presence of shock and/or heart failure.

Publication of series of cases in sufficient detail would help to answer many still unresolved questions concerning optimum time for initiation of pacing, optimum duration of pacing, the length of time the catheter should remain in situ, and the optimum pacing rate.

Submitted by Jacob B. Dana, M.D., Maine Heart Association.
Reference: American Heart Journal, Volume 80, Pages, 116-124, 1970.

Necrologies

Allan D. Craig, M.D.

1884-1970

Allan D. Craig, M.D., 86, of Pacific Grove, California died on April 24, 1970. He was born in Russell, Ontario, Canada on April 4, 1884, son of Thomas Allan and Amanda Craig.

Dr. Craig received his medical degree from McGill University Faculty of Medicine in 1908. He interned at the Royal Victoria Hospital in Montreal from 1909 to 1910. Dr. Craig practiced medicine in London, Ontario from 1911 to 1919, Halifax, Nova Scotia from 1919 to 1922, was an associate director, American College of Surgeons from 1922 to 1927 and medical director at the Charlotte Hungerford Hospital in Torrington, Connecticut from 1931 to 1937. In 1937, Dr. Craig located in Bangor and was medical director at the Eastern Maine General Hospital from 1937 to 1945, and then moved to Pacific Grove, California.

He was an honorary member of the Penobscot County Medical Association and the Maine Medical Association, having received a fifty-year pin in 1958, a fifty-five year pin in 1963 and a sixty-year pin in 1968. He was also a member of the American Medical Association, a charter fellow of the Board of Regents of the American College of Hospital Administrators, a past president of the Connecticut State Hospital Association and a past chairman of the administration section of the American Hospital Association.

John E. Whitworth, M.D.

1904-1970

John E. Whitworth, M.D., 66, of Bangor, Maine died on June 30, 1970. He was born in Smith Falls, Ontario, Canada on March 16, 1904, son of Charles Henry and Mary Emma Whitworth.

Dr. Whitworth was graduated from the University of British Columbia in 1924 and received his medical degree from McGill University Faculty of Medicine in 1928. He interned at the Montreal General Hospital from 1928 to 1929 and served a residency there from 1932 to 1934. In 1934, Dr. Whitworth located in Bangor and practiced there for thirty-six years.

He was a member and past president of the Penobscot County Medical Association, a member of the Maine Medical Association and the American Medical Association. He was also a past president of the New England Ear, Nose and Throat Society, a member of the American Academy of Ophthalmology and Otolaryngology, the American College of Surgeons, the Medical Council of Canada, the Bangor Medical Club, and was Senior Attending Physician of Otolaryngology at the Eastern Maine General Hospital and St. Joseph Hospital and Consultant at the Waldo County Hospital.

Surviving are his widow, Mrs. Marguerite Whitworth; one son, John M. of Huntington, West Virginia; two daughters, Mrs. Frank Pluta of Topeka, Kansas and Mrs. Roger Wing of Farmington; one brother, Dr. Charles Whitworth of Vancouver, British Columbia; three sisters, Mrs. Howard Crawford and Miss Ethel Whitworth, both of Vancouver, British Columbia, and Mrs. Jean Price of Windsor, Ontario; and eleven grandchildren.

Horace L. Gauvreau, M.D.

1888-1970

Horace L. Gauvreau, M.D., 81, of Lewiston, Maine died on May 24, 1970. He was born in Burlington, Vermont on September 2, 1888, son of Louis J. and Lena P. Gauvreau.

Dr. Gauvreau was graduated from the University of Vermont in 1908 and received his medical degree from the University of Vermont College of Medicine in 1912. He interned at the St. Mary's General Hospital in Lewiston from 1912 to 1913, and practiced in Lewiston for fifty-eight years. Dr. Gauvreau was assistant surgeon at the St. Mary's General Hospital from 1915 to 1922, senior surgeon from 1923 to 1936, assistant orthopedic surgeon from 1935 to 1936 and chief of orthopedic surgery from 1937 until his death.

He was an honorary member of the Androscoggin County Medical Association and the Maine Medical Association, having received a fifty-year pin in 1962 and a fifty-five year pin in 1967. He was also a member of the American Medical Association, the Maine Trauma Committee, and was a fellow of the American College of Surgeons and one of the founders of that organization.

Surviving are his widow, the former Maria Louise Lebel; two daughters, Mrs. V. Paul McCauley of Roslyn Heights, New York and Mrs. Charles Dorin of Valley Cottage, New York; one son, Dr. Norman O. Gauvreau of Lewiston; one sister, Mrs. Joseph Judge of Washington, D.C.; and eleven grandchildren.

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The neighbors are wonderful.

Indications: For use in management of anxiety and tension occurring alone or as accompanying symptom complex to medical and surgical disorders and procedures. Though not a hypnotic, fostors normal sleep through antianxiety and related muscle-relaxant properties

Contraindications: History of sensitivity to meprobamate

Important Precautions. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use has been reported to result in dependence or habituation in susceptible persons, as alcoholics, ex-addicts, and other severe psychoneurotics After prolonged excessive dosage, reduce dosage gradually to avoid possibly severe withdrawal reactions. Abrupt discontinuance of excessive doses has sometimes resulted in epileptiform seizures

Warn patients of possible reduced alcohol tolerance, with resultant slowing of reaction time and impairment of judgment and coordination

Reduce dose if drowsiness, ataxia or visual disturbance occurs; if persistent, patients should not operate vehicles or dangerous machinery

Side Effects include drowsiness, usually transient, if persistent and associated with ataxia, usually responds to dose reduction, occasionally concomitant CNS stimulants (amphetamine, mephentermine sulfate) are desirable. Allergic or idiosyncratic reactions are rare, but such reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate Previous history of allergy may or may not be related to incidence of reactions. Mild reactions are characterized by itchy urticarial or erythematous maculopapular rash, generalized or confined to groin Acute nonthrombocytopenic purpura with cutaneous petechiae, ecchymoses, peripheral edema and fever have been reported. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia Treat symptomatically as with epinephrine, antihistamine and possibly hydrocortisone Aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia have occurred rarely, almost always in presence of known toxic agents. A few cases of leukopenia, usually transient, have been reported on continuous administration

Meprobamate may sometimes precipitate grand mal attacks in patients susceptible to both grand and petit mal. Extremely large doses can produce rhythmic fast activity in the cortical pattern. Impairment of accommodation and visual acuity has been reported rarely After excessive dosage for weeks or months, withdraw gradually (1 or 2 weeks) to avoid recurrence of pretreatment symptoms (insomnia, severe anxiety, anorexia). Abrupt discontinuance of excessive doses has sometimes resulted in vomiting, ataxia, tremors, muscle twitching and epileptiform seizures. Prescribe very cautiously and in small amounts for patients with suicidal tendencies Suicidal attempts have resulted in coma, shock, vasomotor and respiratory collapse and anuria. Excessive doses have resulted in prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and occasionally hyperventilation. Treat with immediate gastric lavage and appropriate symptomatic therapy. (CNS stimulants and pressor amines as indicated). Doses above 2400 mg./day are not recommended

Composition. Tablets, 200 mg. and 400 mg meprobamate. Coated Tablets, WYSEALS* EQUANIL (meprobamate) 400 mg (All tablets also available in REDIPAK* (strip pack). Wyeth.) Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

The young homemaker her underlying anxiety and tension can surface and intensify under the continuous stress of rearing a growing family Especially when she's confined to the home ar its environs so much.

You can help her over the rough spots with reassurance and couns Equanil can help relieve tension, ease anxiety—with little risk of serious side effects. Time and experience will probabl do the rest.

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Orenzyme® Bitabs One tablet q.i.d.
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Reduces swelling
Hastens healing
Speeds recovery

trauma

One tablet q.i.d.

Indications: When used as adjunctive therapy for the rapid resolution of inflammation and edema, good results have been obtained in:
☐ Accidental Trauma ☐ Postoperative Tissue Reactions. Other conventional measures of treatment should be used as indicated. In infection, appropriate anti-infective therapy should be given.
Contraindications: ORENZYME BITABS should not be given to patients with a known sensitivity to trypsin or chymotrypsin.
Precautions: It should be used with caution in patients with abnormality of the blood clotting mechanism such as hemophilia, or with severe hepatic or renal disease. Safe use in pregnancy has not been established.
Adverse Reactions: Adverse reactions with ORENZYME have been reported infrequently. Reports include allergic manifestations (rash, urticaria, itching), gastrointestinal upset and increased speed of dissolution of animal-origin surgical sutures. There have been isolated reports of anaphylactic shock, albuminuria and hematuria. Increased tendency to bleed has also been reported but, in controlled studies, it has been seen with equal incidence in placebo-treated groups. (See Precautions.) It is recommended that if side effects occur medication be discontinued.
Dosage: One tablet q.i.d.

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TRADEMARK BITABS U.S. PATENT NO. 3,004,893 9/70 0-009A 161

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Cream (aminacrine hydrochloride 0.2%, sulfanilamide 15.0%, allantoin 2.0%)

Suppositories (aminacrine hydrochloride 0.014 Gm., sulfanilamide 1.05 Gm., allantoin 0.14 Gm.)

Contraindications: Known sensitivity to sulfonamides.
Precautions/Adverse Reactions: The usual precautions for topical and systemic sulfonamides should be observed because of the possibility of absorption. Burning, increased local discomfort, skin rash, urticaria or other manifestations of sulfonamide toxicity are reasons to discontinue treatment.
Dosage: One applicatorful or one suppository intravaginally once or twice daily.
Supplied: Cream—Four-ounce tube with or without applicator. Suppositories—Box of 12 with applicator.

TRADEMARK: AVC AV-007A 7/70 Y-149

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Precautions: Use may result in overgrowth of nonsusceptible organisms. Constant observation is essential. If new infections appear, take appropriate measures. Use of tetracycline during teeth development may cause discoloration of teeth.
Side Effects: Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes (a case of exfoliative dermatitis has been reported); photosensitivity reaction, onycholysis and discoloration of nails (rare). Kidney—rise in BUN, apparently dose-related. Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. In young infants, bulging fontanels have been reported following full therapeutic dosage. This symptom has disappeared rapidly when drug is discontinued. Teeth—dental staining (yellow-brown) in children of mothers given tetracycline during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. Blood—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. Liver—cholestasis (rare), usually at high dosage. Tetracycline may form a stable calcium complex in bone-forming tissue. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy.
Average Adult Daily Dosage: One Gm. per day, in 4 divided doses of 250 mg. each. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

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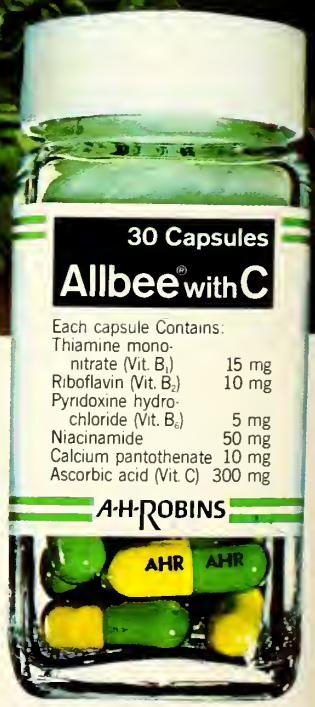

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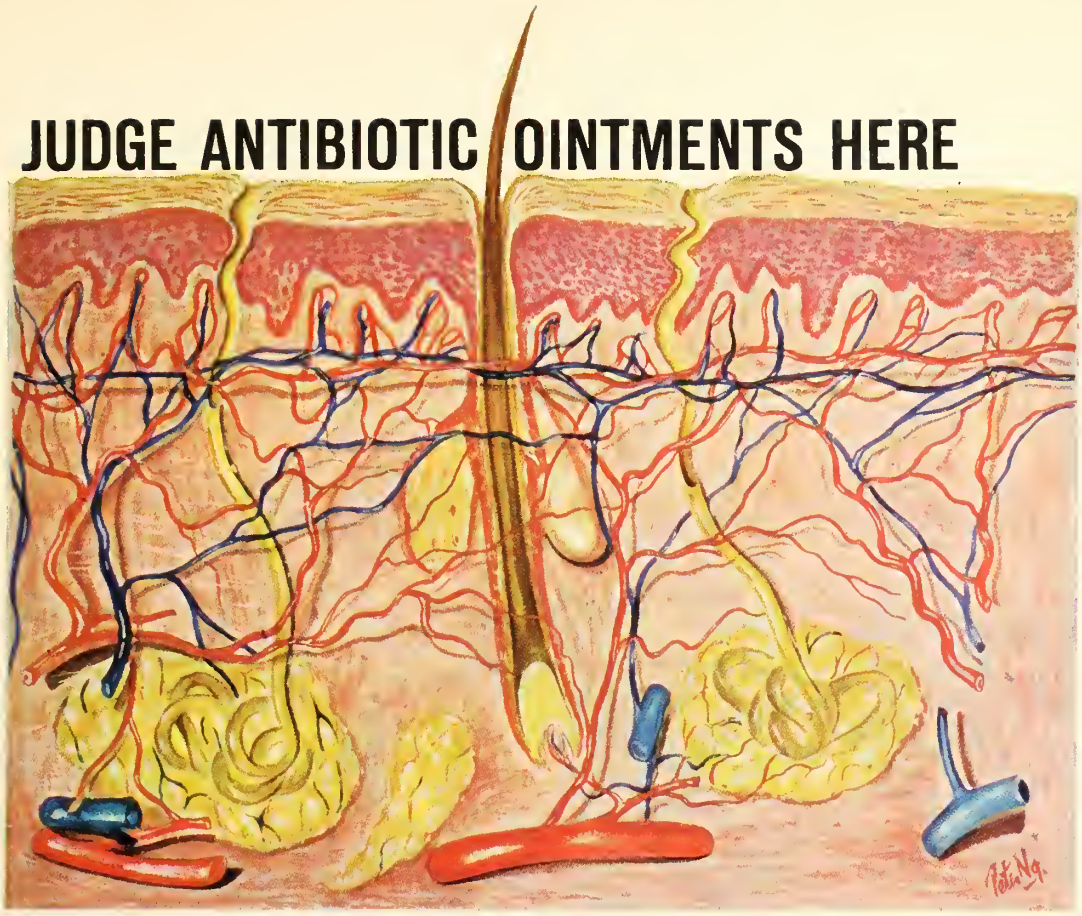

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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.
Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 1 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of Th peutics, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Kestler C., and Gyurik, J.: Industr. Med. S *31*:372, 1962. 4. Forster, S., *et al.*: Ar J. Orthop. *2*:285, 1960. 5. Friend, D. Clin. Pharmacol. Ther. *5*:871, 1964.

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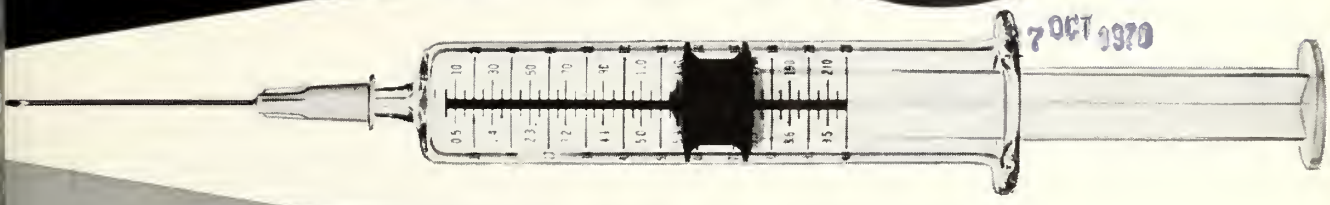

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* PATRICIA A. BERGERON, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

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Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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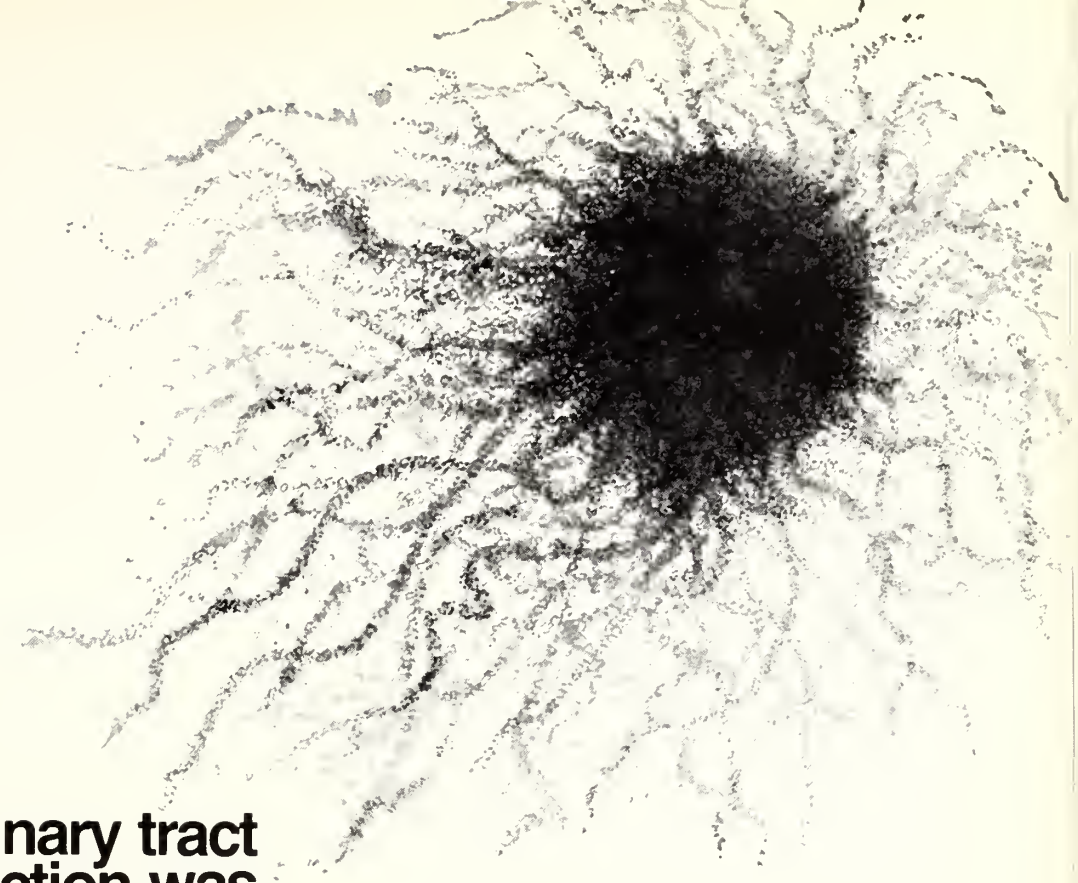

A urinary tract infection was eliminated last week

ntestinal monilial overgrowth has appeared this week

For women who are diabetic or debilitated, oral antibiotic therapy often sets the stage for monilial overgrowth in the intestine.

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Contraindication: History of hypersensitivity to demethylchlortetracycline or nystatin.

Warning: In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

Precautions: Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects: Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes; a rare case of exfoliative dermatitis has been reported. Photosensitivity, onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose-related. Transient, reversible, nephrogenic diabetes insipidus with excessive thirst and polyuria (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth—dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs, discontinue medication and institute appropriate therapy. Demethylchlortetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans.

Average Adult Daily Dosage: One tablet b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

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mptoms. This means the symptoms
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Indications: Management of manifestations generally associated with the menopausal syndrome—anxiety and tension, vasomotor complaints and hormonal deficiency states.

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Precautions: In elderly and debilitated patients, limit dosage to smallest effective amount of chlordiazepoxide (initially 10 mg or less per day) to preclude ataxia or oversedation; increase gradually as needed and tolerated. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects—particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in patients with impaired renal or hepatic function. Paradoxical reactions to chlordiazepoxide (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in the treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation very rarely reported in patients receiving Librium® (chlordiazepoxide) and oral anticoagulants.

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With estrogens, headache, nausea and vomiting, anorexia, gastrointestinal discomfort, dysuria and urinary frequency, jitteriness, breast engorgement, formation of breast cysts, skin rashes and pruritus occasionally seen. Administration may also be associated with uterine bleeding and/or followed by withdrawal bleeding.

Usual Dosage: One tablet t.i.d. for 21 days, followed by one-week rest periods.

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5 mg chlordiazepoxide	5-4	0.4 mg water-soluble esterified estrogens
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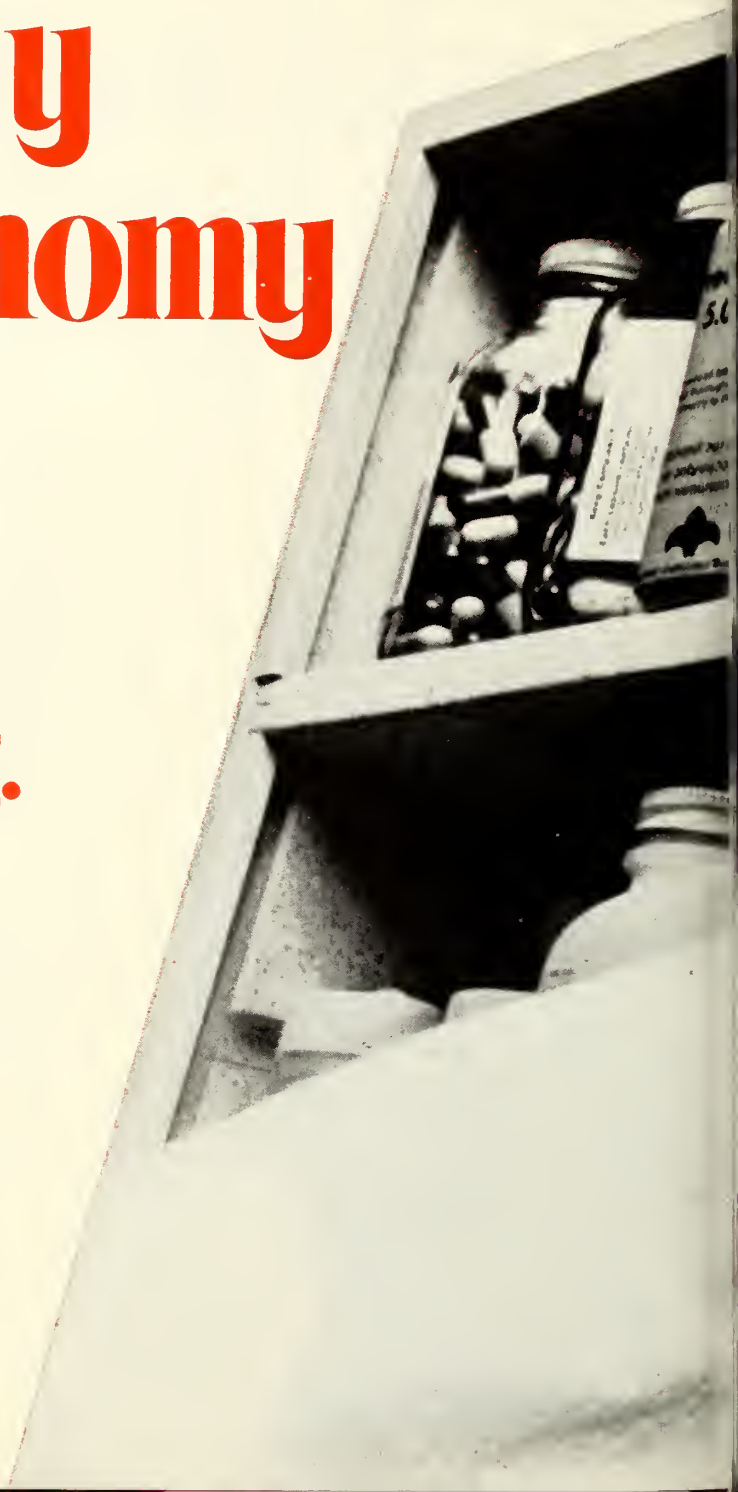

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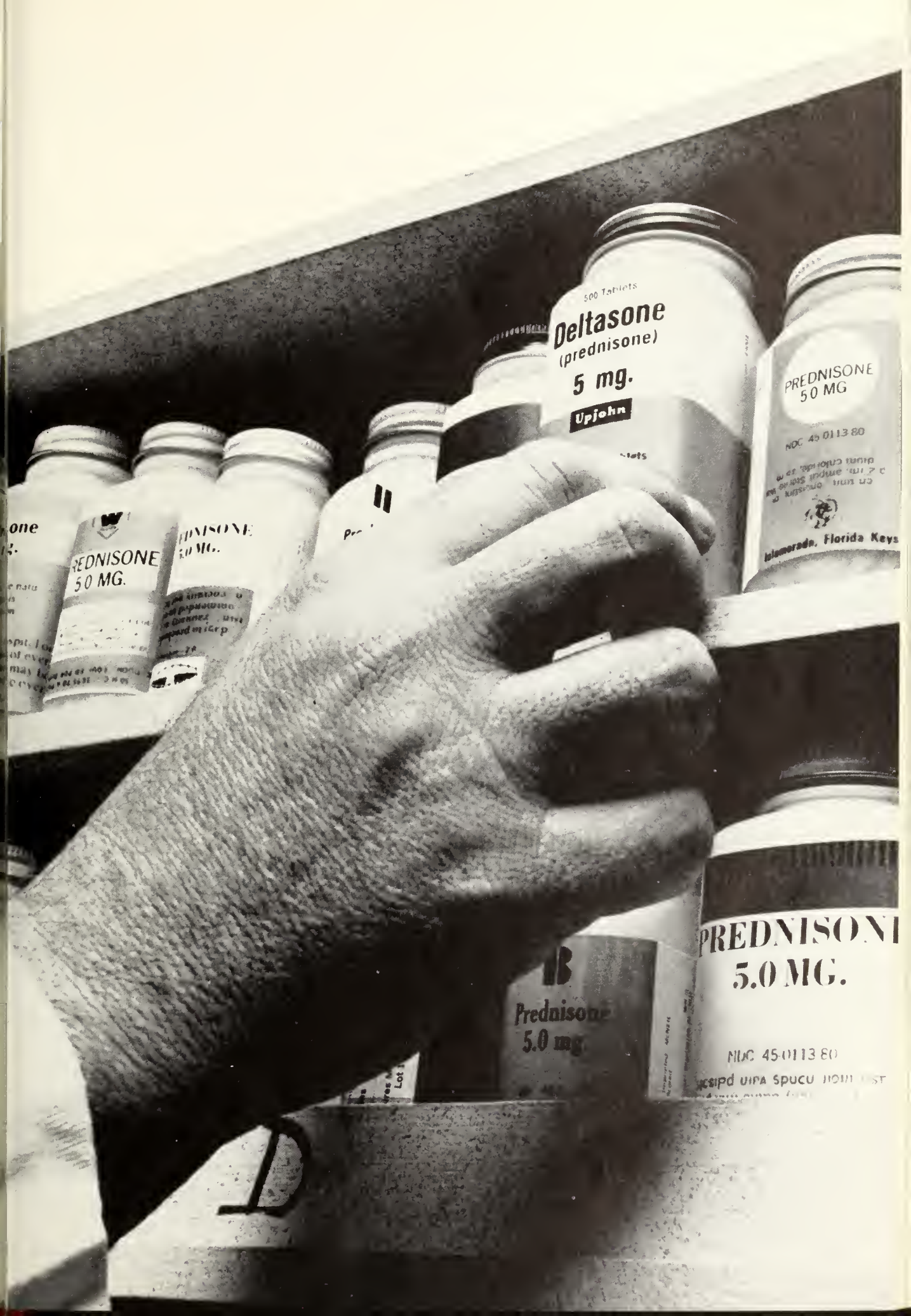
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The potency of prednisone exceeds cortisone in glucocorticoid and anti-inflammatory activity by about five times on a weight basis, but is considerably less active than cortisone in mineralocorticoid activity.

Indications are the same as those for other anti-inflammatory steroids. Representative uses include collagen diseases, allergic diseases, generalized dermatoses, acute ocular inflammatory disease, certain lymphatic neoplastic diseases, ulcerative colitis and nephrosis. *Important:* Prednisone, like cortisone, is a potent therapeutic agent influencing the biochemical behavior of most, if not all, tissues of the body. Because it manifests little sodium-retaining activity, the usual early sign of cortisone overdosage (i.e., increase in body weight due to fluid retention) is not a reliable index. Hence, recommended dose levels should not be exceeded, and all patients should be under close medical supervision. All precautions pertinent to the use of cortisone apply to Deltasone (prednisone).

Contraindications: As for all other corticoids. *Considered Absolute*—herpes simplex keratitis, acute psychoses and latent, healed or active tuberculosis. May be lifesaving in certain cases of pulmonary or meningeal tuberculosis, but should be used only in conjunction with adequate and effective antituberculous therapy to which causative organisms are shown to be sensitive. *Considered Relative*—active or latent peptic ulcer, Cushing's syndrome, diverticulitis, fresh intestinal anastomoses, osteoporosis, renal insufficiency, thromboembolic tendencies, psychotic tendencies, diabetes mellitus, hypertension, local or systemic infections including vaccinia, varicella and other exanthematous diseases, and fungal infections, and, pregnancy particularly during the first trimester because of observation of fetal anomalies in experimental animals. If necessary to give corticosteroids during pregnancy, watch newborn infants closely for signs of hypoadrenalism and institute appropriate therapy if signs appear.

If corticoids are used in the above conditions, weigh risks against benefits.

Precautions: Deltasone should be given only with full knowledge of characteristic activity of and varied responses to corticoids. Because of inhibiting effect on fibroplasia, corticoids may mask signs of and enhance spread of infection; hence, watch patients closely, and if intercurrent infection occurs, control with appropriate antibacterial measures. If possible, avoid abrupt cessation of corticosteroid therapy because of the danger of superimposing adrenocorticoid insufficiency on the infectious process. Prolonged hormone therapy usually causes a reduction in the activity and size of the adrenal cortex. When discontinuing therapy, relative adrenocortical insufficiency may be avoided by gradual reduction of dose. However, a potentially critical degree of insufficiency may persist asymptomatically for some time even after gradual discontinuation of adrenocortical steroids. Therefore, if a patient is subjected to significant stress, such as surgery, trauma, or severe illness while being treated, or within one year (occasionally up to two years) after treatment has been terminated, hormone therapy should be augmented or reinstituted and continued for the duration of the stress and immediately following it. Since mineralocorticoid secretion may be impaired, salt and/or desoxycorticosterone should be administered conjunctively. It is preferable to use a soluble hormone preparation in the immediate preoperative and postoperative periods.

Although unlikely with Deltasone, average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary. Glucocorticoid steroids may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestations of latent diabetes mellitus may be precipitated. Corticosteroids may aggravate myasthenic symptoms in myasthenia gravis and should be given with proper precautions.

Muscle weakness, in some instances, attributed to hypopotassemia, has been reported following prolonged systemically administered corticoids. Excessive potassium loss, like excessive sodium retention, is not likely to be induced with effective maintenance doses of Deltasone (prednisone), however, keep this eff in mind and perform periodic serum potassium determinations patients on prolonged corticoid therapy. Muscle weakness occ ring with normal serum potassium levels may be due to disturbar in muscle metabolism. Severe myopathy is associated with st stantial doses of steroids for prolonged periods, and evider indicates it occurs more frequently with 9-alpha-fluro steroids. F placement with non-fluorinated steroid has, in some instances, sulted in improvement.

Retardation of linear growth, roughly proportional to dose, h been noted in children on corticoids for six months or more. Follc ing cessation of therapy, growth rate may be accelerated. The fore, carefully observe growth of children on prolonged cortic and if growth is retarded, reduce dose sufficiently to permit recov before epiphyseal closure. Make every effort to avoid cortico during pregnancy, since spontaneous remission of some diseas such as rheumatoid arthritis may occur. Long term corticoid thera may evoke hyperacidity or peptic ulcer, therefore, as prophylax an ulcer regimen and antacid are highly recommended. Take X-ra in peptic ulcer patients complaining of gastric distress, ar whether or not changes are noted, an ulcer regimen is reco mended. Since prednisone causes less salt and water retenti than many other glucocorticoids, patients should be observ closely for development of undesirable hormonal effects that a less obvious indications of steroid toxicity than edema and hype tension due to salt and water retention. Continued supervision patients after cessation of therapy is essential, since there may l a sudden reappearance of severe disease manifestation.

Adverse Reactions: Adverse reactions associated with use of cor coids include: Cushing's syndrome, moon facies, supraclavicul fat pads, hirsutism, striae and acne; relative adrenocortical insuf ciency particularly in time of stress due to trauma, surgery severe illness; protein catabolism with negative nitrogen balanc electrolyte imbalance; alteration of glucose metabolism with aggr vation of diabetes mellitus including hyperglycemia and glycosuri osteoporosis reversible only with difficulty; spontaneous fracture aseptic necrosis of the hip and humerus; activation and complic tion of peptic ulcer including perforation and hemorrhage; aggr vation or masking of infection; increased blood pressur convulsions; petechiae and purpura; menstrual irregularities i cluding amenorrhea, spotting or prolonged bleeding; insomni psychic disturbances especially abnormal euphoria; nervousnes posterior subcapsular cataracts occasionally requiring extractio increased intraocular tension; increased intracranial pressure wi papilledema (pseudotumor cerebri); pancreatitis; necrotizing ang itis; thinning of scalp hair; suppression of growth in childre thromboembolic complications; facial erythema; allergic skin rea tions; ulcerative esophagitis; sweating; vertigo; weakness; myop athy; headache; exophthalmos. Adverse reactions are usual reversible and usually disappear when drug is discontinued.

Supplied: 2.5 mg., scored—bottles of 100 tablets. 5 mg., scored bottles of 100 and 500 tablets and cartons of 100 tablets in fc strips.

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Deltasone® 5 mg. (prednisone, Upjohn)

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Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause CNS *effects* such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported. Sympathomimetic *cardiovascular effects* reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others. *Allergic phenomena* reported include such conditions as rash, urticaria, ecchymosis, and erythema. *Gastrointestinal effects* such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tablet daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet three times daily, one hour before meals. If desired, an additional tablet may be given in midevening to overcome night hunger. Use in children under 12 years of age is not recommended.

T-006A / 1/70 / U.S. PATENT NO. 3,001,910

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One thing patients can sleep without, particularly patients with chronic disease conditions such as arthritis, diabetes or PVD, is painful night leg cramps. Although seldom the presenting complaint, night leg cramps can tie your patients up in painful knots. Now, just one tablet of QUINAMM at bedtime can usually bring an end to shattered sleep and needless suffering. Your patients will sleep restfully—gratefully—with QUINAMM, specific therapy to prevent painful night leg cramps.

Prescribing Information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions/Adverse Reactions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastraintestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

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In Witness Whereof Associated Hospital Service of Maine (a Non-profit Maine Corporation) has duly executed this Contract.

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PHYSICIAN SERVICE

Article I Definitions

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The Journal
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Volume Sixty-one | Brunswick, Maine, October 1970 | Number 10

The Diagnosis and Management of Common Thyroid Diseases*

HERBERT A. SELENKOW, M.D.** and NOEL I. ROBIN, M.D.***

INTRODUCTION

The past decade has seen a host of significant changes in the diagnosis and treatment of thyroid disease. Advanced techniques, especially in the analysis of serum thyroid hormone parameters, now enable the physician to make more precise and more definitive diagnoses. Thus, treatment of thyroid disease, whether it be related to functional derangements or to the goitrous state, has become more distinctly delineated by rather specific and succinct guidelines for each pathologic condition.

It is the purpose of this brief review to condense the wealth of recently acquired material into a general perspective of thyroid knowledge and to produce a meaningful and relevant approach to thyroid diagnosis and treatment. It is not our intent, nor should it be, to be overly technical or biochemical – there are certainly sufficient reference materials and texts available for that purpose. Our major aim is to summarize and hopefully, to clarify some common and clinically useful aspects of thyroid problems encountered in general medical practice.

For clarity and maximal understanding, this review is divided into four major sections: I. Diagnosis of thyroid disease using available tests of thyroid function; II. The hyperthyroid state; III. The hypothyroid state; and IV. The goitrous state. A brief question and answer discussion, derived from the audience participation at the Fall Symposium on Diseases of the Thyroid, held at St. Mary's Hospital, Lewiston, Maine, October 29, 1969, follows the end of this review.

THE DIAGNOSIS OF THYROID DISEASE USING AVAILABLE TESTS OF THYROID FUNCTION

Before specific tests can be discussed, it is important that some basic thyroid physiology be understood. Without this understanding, values for these tests become meaningless numbers and underlying concepts cannot be applied appropriately. For all practical purposes, thyroid hormonal physiology can be divided into three major stages. There are appropriate categories of tests of thyroid function for each of these physiologic subdivisions (Fig. 1). The first category relates to the thyroid-pituitary axis, the second to transport of circulating thyroid hormones and the third to hormonal actions on peripheral tissues.

The thyroid-pituitary axis can be likened to a closed feedback loop. Through hypothalamic and higher centers, the pituitary gland elaborates a thyrotropic hormone (TSH) which stimulates the thyroid gland to both synthesize and secrete thyroxine (T4) and triidothyronine (T3), the two major thyroid hormones. These hormones, once released from the thyroid, circulate in the blood and ultimately reach all metabolically active tissues. Depending upon their ultimate concentrations, the pituitary either suppresses or releases TSH. When the blood thyroid hormone levels are low, as in hypothyroidism, significant amounts of TSH are elaborated. Conversely, serum levels of TSH are virtually undetectable in the presence of increased amounts of circulating thyroid hormones. This particular system in thyroid gland physiology (Table 1) is commonly measured by using the 24-hour radioactive iodine uptake test (RaI) depicted graphically in Fig. 2. The patient is given a tracer drink of radioactive iodine (usually ^{131}I) and 24 hours

*This article represents an edited version of a series of lectures presented at the Fall Symposium on Diseases of the Thyroid on October 29, 1969, at St. Mary's General Hospital, Lewiston, Maine 04240.

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***Postdoctoral Research Fellow in Endocrinology, Peter Bent Brigham Hospital and Harvard Medical School.

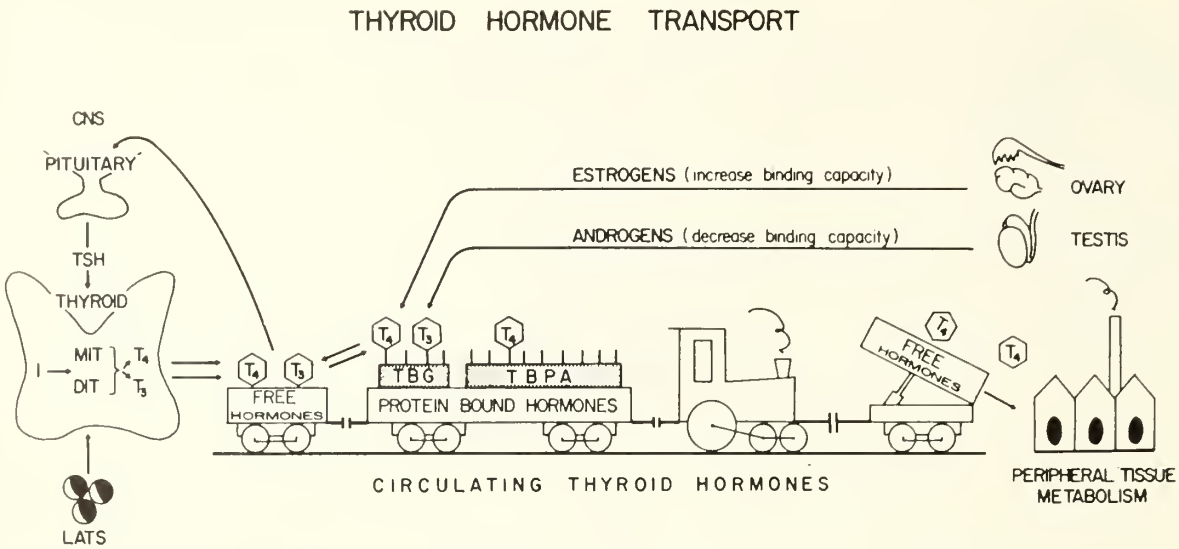

Fig. 1. Diagrammatic representation of thyroid hormone synthesis and secretion, transport in the circulation and peripheral effects. Tests measuring the relationships between the pituitary and thyroid (pituitary-thyroid axis), serum levels of bound and free thyroid hormones, and cellular actions of thyroid hormones are described in the text and listed in Table 1.

later, his thyroid gland is counted for residual radioactivity. Normally, approximately one-third (range: 15-45%) of the ingested isotope remains in the thyroid gland at 24 hours. As originally intended, this test measures the total activity of the thyroid gland. In the presence of an underactive gland, whether of primary etiology or secondary to hypopituitarism, the RaI is low (usually less than 15%). Conversely, hyperthyroidism is often associated with a high RaI (generally above 50%). The latter state is commonly mediated by one of two mechanisms. On one hand, the thyroid gland can become autonomous and produce thyroid hormones uncontrollably and independent of the influence of pituitary TSH. This thyrogenic disorder usually occurs in the so-called toxic nodular goiter, or Plummer's disease. Thyrotoxicosis due to toxic nodular goiter occurs most frequently in the older age groups and frequently manifests myopathic and cardiovascular symptomatology. Another quite distinct mechansim occurs in Graves' disease. This is a systemic disorder mediated by a circulating abnormal protein known as the "long acting thyroid stimulator" (LATS). This 7S gamma globulin is an antibody-like plasma protein produced by the reticuloendothelial system that has an intrinsic TSH-like action on the thyroid gland. It, too, circulates autonomously and is not under feedback regulation by serum levels of thyroid hormones. Regardless of which of these etiologies is responsible, the net result is an increased RaI uptake by the thyroid gland.

The RaI, while a useful test, is not without its pitfalls. The commonest source of error is due to exogenous iodide interference. The rationale of this test relies upon the inability of the thyroid gland to distinguish radioactive from stable (non-radioactive) iodide and hence to trap radioactive iodine with affinity equivalent to its ability to trap stable iodine. Thus, an increased supply of circulating stable iodide could render the thyroidal radioactive uptake significantly low. Sources of this iodide are increasing daily and range from bread to Betadine® (used as a swimming pool germacide) to a host of roentgenologic contrast materials. The latter are of particular significance because of their associated long biological half-lives. Dyes used in bronchography may have a half-life of a year or more and those used in myelography may last for decades. Conversely, a state of relative iodine deficiency may falsely increase the RaI uptake. Such conditions occur in starvation, enteropathies and the nephrotic syndrome. If renal disease becomes severe, the RaI may then be elevated further because the kidneys, which normally excrete the iodine not trapped by the thyroid gland, cannot perform this function. Several congenital diseases of thyroid metabolism and even some goitrous states (such as Hashimoto's thy-

TABLE 1

COMMON CLINICAL TESTS OF THYROID FUNCTION

A. *Thyroid-Pituitary Axis*
   1. Radioactive Iodine Uptake
   2. Thyroid Suppression
   3. TSH Stimulation
   4. Radioiodine Tests of Intra-Thyroidal Iodine Metabolism
B. *Thyroid Hormone Transport*
   1. Tests measuring total serum T4: T4D, PBI, BEI, T4Ic
   2. Tests measuring unbound TBG: Resin-T3 (RT3), Resin-T4 (RT4), Erythrocyte-T3 (ET3)
   3. Free Thyroxine Index (FTI-T3 or FTI-T4)
   4. Free Thyroxine by Dialysis (FT4)
C. *Tissue Oxidative Actions*
   1. Basal Metabolic Rate (BMR)
   2. Achilles Tendon Reflex; EKG Changes
   3. Serum Enzymes (CPK, LDH)
   4. Cholesterol; Creatine Tolerance

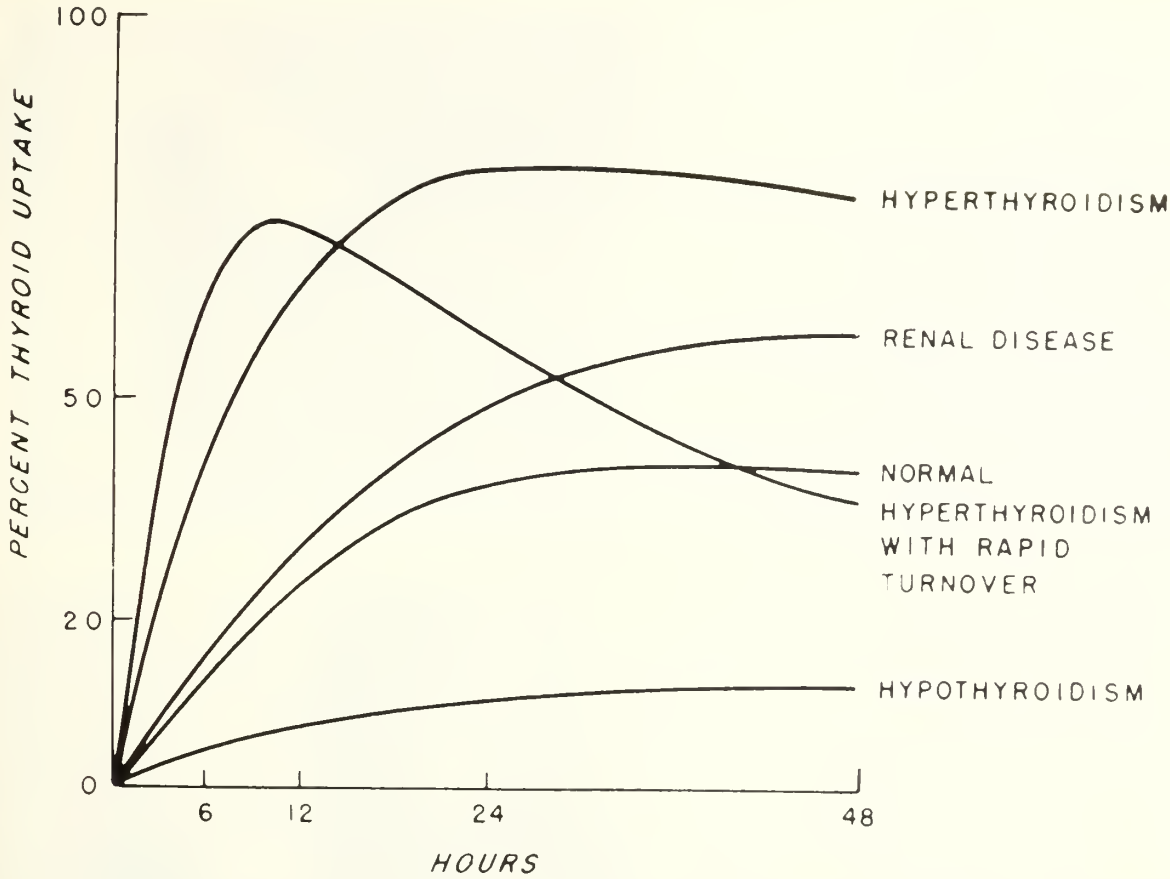

Fig. 2. Representative curves for the thyroidal uptake of radioactive iodine (Means, J. H., DeGroot, L. J. and Stanbury, J. B.), *The Thyroid and its Diseases*, 3rd ed., McGraw-Hill, New York, 1963.

roiditis) can give falsely elevated RaI values. This is because of interferences with thyroid hormone synthesis and secretion resulting in decreased serum thyroxine (T4) levels. The pituitary responds only to circulating thyroid hormones and thus excess amounts of TSH are produced in an effort to compensate for the T4 deficiency. This, in turn, causes over-stimulation of the thyroid gland in an attempt to meet peripheral demands. Of final interest, the 24-hour RaI in severe hyperthyroidism may occasionally be normal or even low (Fig. 2). In such a situation, the thyroid is so overactive that it has rapidly incorporated radioactive iodine, made thyroxine (T4) and triiodothyronine (T3) from it, and released it in less than a day. In these patients, a six hour uptake shows a high degree of thyroidal radioactivity, but these patients are so toxic clinically that this added step to the standard RaI is generally not necessary for diagnostic purposes.

Two variants of the RaI uptake test are the thyroid scan and the thyroid suppression test. The former (Fig. 3) renders a graphic delineation of the thyroid anatomic configuration and is often of importance when looking for goiter or nodules. The latter (Fig. 4), the thyroid suppression test, measures the autonomy of the pituitary-thyroid axis. One of the basic principles of the endocrine system, the thyroid being no exception, is to be autoregulated by a servo-mechanistic feedback system. One would thus expect that if an individual is given sufficient exogenous thyroid hormones to maintain adequate circulating levels, the endogenous production of thyroid hormones should be curtailed. Indeed, if a normal individual is placed on L-triiodothyronine (liothyronine, Cytomel®), 75-100 mcg. daily for seven days (the standard T3 suppression test dosage and time period), one would expect his RaI to fall from normal to below normal values. And this, indeed, is what generally occurs in normal subjects (Fig. 4). The hyperthyroid state, however, regardless of the etiology, is autonomous and thus, thyroid function as measured by the RaI uptake fails to be suppressed in these patients after a standard time period of T3 ingestion. This test is of greatest value in those individuals with borderline laboratory parameters and ambiguous clinical signs and symptoms in whom the diagnosis is difficult to make. Unfortunately, many such individuals are in the older age groups and often present with thyrocardiac disease. In these individuals, this test, if indeed used at all, must be prudently administered in order not to accelerate the cardiac abnormality or to induce cardiac dysfunction when not present.

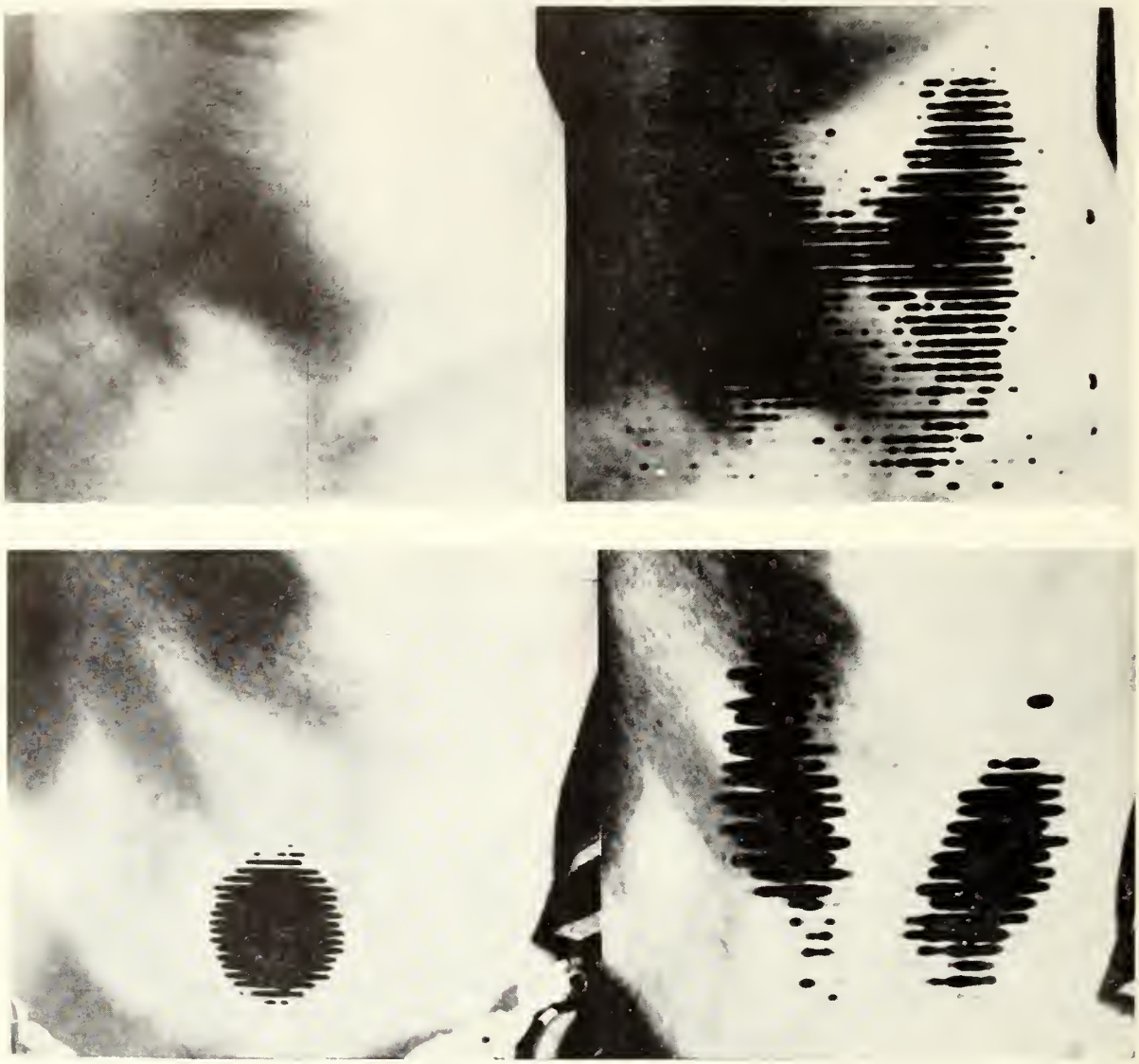

Fig. 3. Representative radioisotopic thyroid scans superimposed upon photographs of the patient's neck. In the upper set, the patient on the left had a solitary thyroid nodule in the lower pole of the left lobe. The scan on the right shows the nodule to be "cold." In the lower set, the scan on the left shows a single "hot" nodule on the lower portion of the right lobe of the thyroid. The scan on the right was taken postoperatively showing resumption of function in the remainder of the normal thyroid. Note the surgical defect ("cold" area) in the lower portion of the right lobe.

The TSH stimulating test is the converse of the suppression test (Fig. 5). Suffice it to say that it is little used today in view of the availability of more precise tests. This topic will be covered more completely under the discussion of the hypothyroid state.

Now that we have surveyed the major tests for assessing the pituitary-thyroid axis, we turn to the section that deals with the circulating thyroid hormones. Returning to Fig. 1, we see schematically that thyroid hormones (T3 and T4), although released from the thyroid gland in their "free" or unbound form, are immediately taken up, within the blood, by specific thyroid binding proteins. In order of affinity for thyroid hormones and physiologic significance, they are thyroxine binding globulin (TBG), thyroxine binding pre-albumin (TBPA) and serum albumin. Although T3 is a physiologically more potent hormone than T4 (about four times as active metabolically as T4), its total serum concentration is only about 1/15 that of T4. The metabolically active moiety of T3 accounts for about half the calorigenic activity of thyroid hormones in serum.

Just as the materials carried by a freight train are of no economic value until they are released into the open market, so the physiologic activity of thyroid hormones is only significant when they are in the "free" state. Thyroxine bound to plasma proteins, although accounting for over 99.9% of the total circulating thyroid hormones, acts mainly as a huge serum reservoir and it is

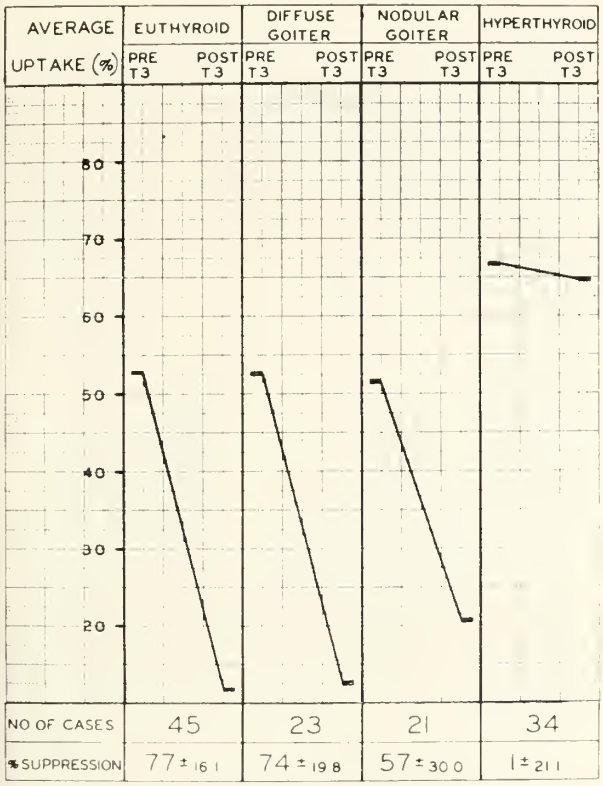

Fig. 4. The Thyroid Suppression Test. Values indicate the 24-hour ^{131}I uptake before and one week after administration of liothyronine 75 micrograms daily by mouth. (Burke, G., Am. J. Med. *42*:600, 1967).

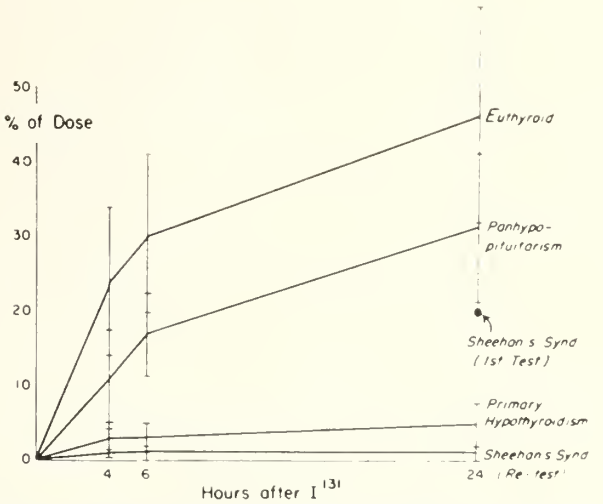

Fig. 5. Thyrotropin Stimulation Test. The effects of a single intramuscular injection of porcine thyrotropin on the 24-hour radioiodine uptake test. The tests in Sheehan's Syndrome are reversed (that is, the 1st test is actually *after* TSH stimulation. (Taunton, O. D., McDaniel, H. B. and Pittman, J. A., J. Clin. Endocrinol. *25*: 266, 1965).

only the "free" T4 moiety of less than 0.1% that exerts a metabolic effect. It is important to emphasize that no matter what happens to the total protein-bound thyroid hormone levels, these changes are without metabolic consequence unless accompanied by concomitant changes in "free" thyroid hormone levels. The serum levels of "free" thyroid hormones determine tissue metabolic status. This concept applies to many hormones such as cortisol, estrogens and androgens all of which circulate in electrostatic equilibrium with specific plasma proteins. *All* the major tests for serum thyroxine (i.e., protein-bound iodine (PBI), butanol extractable iodine (BEI), thyroxine iodine by column (T4Ic) and serum thyroxine by displacement analysis (T4D) are a function of the *total* thyroxine. They reflect the "free" or metabolically significant portion of serum thyroxine only if there are no alterations in the binding proteins (particularly TBG). This important topic will be re-emphasized later in the discussion. For the time being, let us examine why the T4D is presently the most accurate test of these four.

The PBI measures exactly what the name implies: the serum iodine that is specifically bound to plasma proteins. The thyroid gland is unique in that it secretes hormones which incorporate iodine in their molecular structure. Thus, in the normal individual, the PBI should provide an accurate assessment of the total circulating thyroxine iodine. Unfortunately, there are an ever-increasing number of non-hormonal iodine-containing compounds used medicinally or otherwise that significantly alter serum PBI values. If we realize that the PBI range reflects a small concentration of iodine to begin with (4-8 μg/100 ml), one realizes how easy it is to elevate this level by comparatively small amounts of non-hormonal exogenous iodides. These "contaminants" are derived from a variety of sources but the most common offenders are usually roentgenologic contrast materials (particularly significant because many have prolonged biologic half-lives), pharmacologic preparations (SSKI, iodine-containing vitamins, etc.), and antiseptic agents (Betadine, tinctures of iodine, etc.). Further, certain iodinated proteins released into the circulation under pathologic conditions, may be measured by the PBI but do not possess calorigenic properties. The classic example of this is in Hashimoto's thyroiditis (chronic lymphoid thyroiditis) but this phenomenon may also occur in certain goitrous, thyrotoxic and congenital disease states.

The butanol extractable iodine (BEI) was developed in an attempt to separate by extraction the hormonal from non-hormonal iodinated materials. Indeed, the abnormal iodotyrosines and iodoproteins found in such disease states as Hashimoto's thyroiditis are not reflected in the BEI determination. In addition, some amounts of circulating iodide (but *not* the synthetic organic iodine compounds) are also excluded by the BEI procedure. Nonetheless, the previously alluded to exogenous substances that cause false elevations in PBI levels are generally also measured by the BEI and this latter test is thus scarcely better than the former in measuring true levels of circulating thyroxine. The "thyroxine" iodine by column chromatography (T4Ic) was devised in an

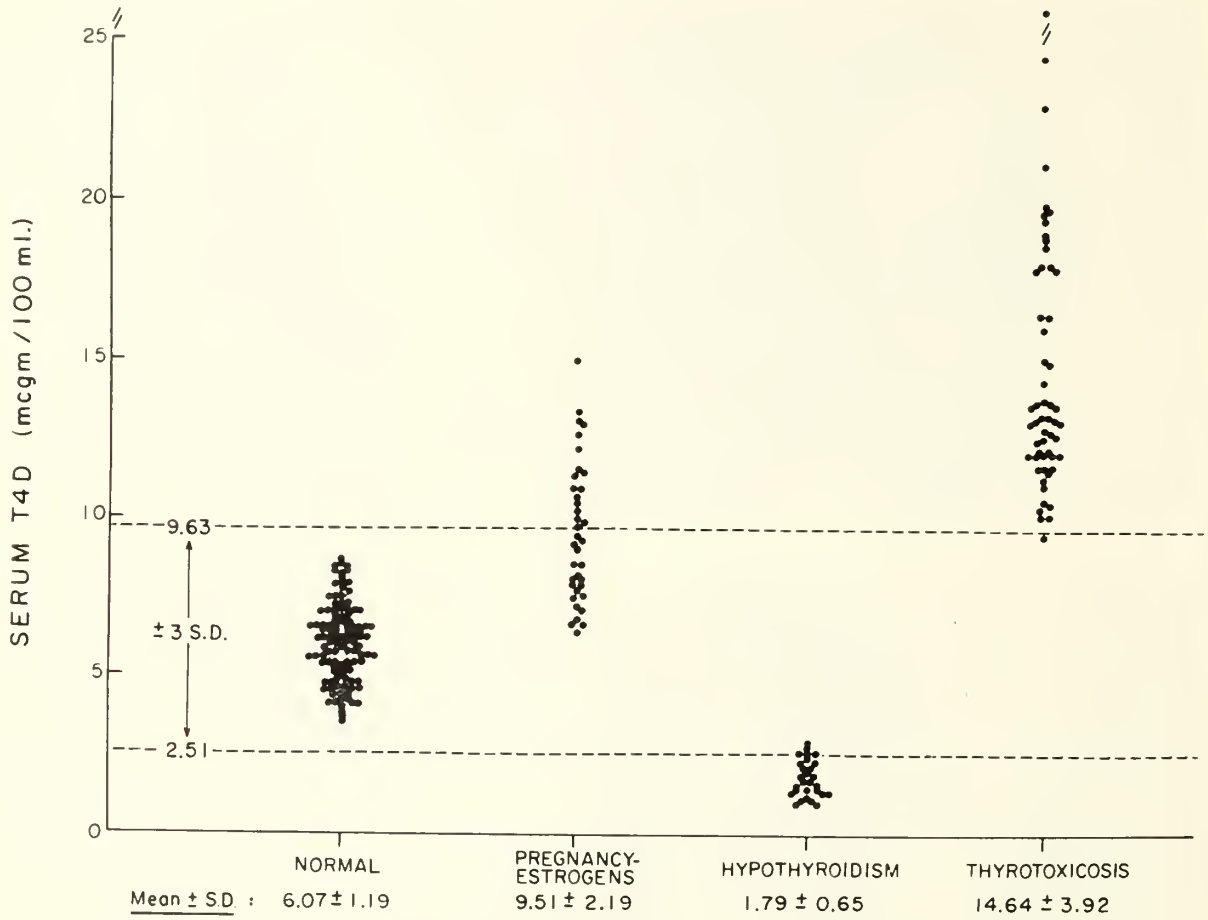

Fig. 6. Values for the T4D (serum thyroxine concentration) in normal subjects and in patients on estrogens or pregnant, hypothyroidism or hyperthyroidism obtained in the Thyroid Laboratory at the Peter Bent Brigham Hospital.

attempt to chromatographically exclude non-hormonal iodinated substances from the iodine determination. While of greater efficiency in this respect than the PBI or BEI, it, too, cannot entirely exclude these contaminants.

The serum thyroxine by displacement analysis (T4D) as developed by Murphy and Pattee, takes cognizance of the fact that the specific thyroid binding protein, TBG, will not bind non-hormonal iodinated substances. For this reason, the T4D has now become the most useful test for measuring serum total thyroxine under a wide variety of clinical circumstances. As this *in vitro* test can be performed with a minimum of isotopic counting equipment, it is rapidly replacing the tests of chemical iodine analysis (PBI, BEI, T4Ic) and is now readily performed by most clinical laboratories. Shown in Fig. 6 and Table 2 are the levels of T4D obtained in our laboratory in normal subjects and in patients with common thyroid disorders. The normal range for this determination, derived from frequency distributions, is 4.0 – 10.0 μg/100 ml. (40-100 ng/ml). Since this test is also done economically and efficiently by a wide variety of commercial laboratories, there is now generally little reason for obtaining serum iodine tests of total thyroxine.

Unfortunately, as previously mentioned, this test measures only *total* thyroxine, and unless the thyroxine binding proteins are present in normal concentrations, the values for the T4D, although an accurate measure of serum T4 levels, may not be a valid reflection of the "free" or metabolically active thyroid hormones. Indeed, a variety of conditions exist which alter serum T4 binding proteins without affecting thyroid metabolism directly. For example, estrogens (as in oral contraceptive agents or pregnancy) stimulate the production of higher circulating levels of TBG. Thus, the *total* serum thyroxine concentration increases but, as will be shown later in this section, the "free" T4 levels remain normal as does the metabolic status of the patient. Conversely, androgens, anabolic steroids and glucocorticoids (to some degree) diminish levels of serum TBG and thus reduce the T4D concentration without ultimately altering levels of free thyroxine. A similar phenomenon is caused by other drugs which do not affect TBG levels directly but rather compete with T4 for the binding sites on TBG or TBPA and, thus, lower the serum T4D levels by this mechanism. Such agents include the hydantoins and salicylates. As in the situations where the TBG concentration is altered, "free" thyroxine under these conditions

TABLE 2

CLINICALLY USEFUL RANGES FOR T4D, RT3 RATIO AND FTI-T3 DERIVED FROM FREQUENCY DISTRIBUTION DATA OBTAINED IN THE THYROID LABORATORY, PETER BENT BRIGHAM HOSPITAL

Diagnostic Category	*T4D μg/100 ml*	*RT3 Ratio*	*FTI-T3*
Hypothyroid	<3	0.5 - 0.8	<3.5
Borderline Low	3-4	0.80 - 0.95	3.5 - 4.5
Euthyroid	4-10	0.95 - 1.15	4.5 - 10.5
Borderline High	10-12	1.15 - 1.26	10.5 - 12.5
Hyperthyroid	>12	>1.26	>12.5

also remains unchanged in the presence of reduced T4D levels.

One way to solve this apparent dilemma is to measure "free" thyroxine (FT4) directly. Indeed, such procedures have been devised and are operative in many laboratories. Unfortunately, these tests are rather elaborate, time-consuming and not generally practical for most clinical laboratories. Further, it will be readily seen from the forthcoming discussion that presently available tests obviate the need to perform a direct determination for "free" thyroxine (FT4) since comparable results can be derived under most circumstances by simpler procedures.

To better understand the physiologic interactions between FT4, TBG and the T4D, let us examine the physical-chemical relationship between thyroxine and its principle circulating protein binder, TBG. This chemical reaction can be expressed mathematically by the following mass action equilibrium equation:

$$\text{FT4} + \text{TBG} \underset{0.04}{\overset{99.96}{\rightleftharpoons}} \text{TBG-T4} \quad \ldots\ldots\ldots\ldots\ldots 1$$

This equation states that "free" T4 (FT4) when reacted with "free" (unsaturated) TBG produces an electrostatically-bound combination (TBG-T4) such that 99.96% of the reaction mixture is TBG-T4 and only 0.04% FT4. Solving for FT4 by the following two steps, we derive a relationship for the mathematical expression of the serum "free" thyroxine concentration (FT4).

$$K = \frac{[\text{TBG-T4}]}{[\text{FT4}]\text{x}[\text{TBG-T4}]} \quad \ldots\ldots\ldots\ldots\ldots 2$$

$$K[\text{FT4}] = [\text{TBG-T4}]\text{x}[\text{TBG}]^{-1} \quad \ldots\ldots\ldots\ldots\ldots 3$$

It is apparent that K[FT4] is a function (index) of the "free" T4 concentration (FT4) and this has been designated the free thyroxine index (FTI). The T4D, for all practical purposes, is the best measure of the total serum thyroxine and can be used as a test of the factor [TBG-T4]. The PBI, BEI or T4Ic (Table 1 and Fig. 7) could also be used for this but are less useful in this regard as

FREE THYROXINE INDEX (FTI) =

[TBG – T4] *(Serum total T4)*	X	$[\text{TBG}]^{-1}$ *(1/ unbound TBG)*
T4D		Resin T3 (RT3)
PBI, BEI		Resin T4 (RT4)
T4Ic		Dialysable Fraction (D.F.)

Fig. 7. Common laboratory tests of thyroid function used to measure serum total T4 and unbound TBG. These factors can be used in formula 3 of the text to calculate the various free thyroxine indices.

discussed previously. Shown in Fig. 7 is a simplified version of equation 3 with clinical tests used for deriving the FT4 or FTI.

There are, similarly, several available tests for measuring the factor $[\text{TBG}]^{-1}$ (Table 1, Fig. 7). The most commonly available of these is known as the resin-T3 uptake test (RT3) (Fig. 8). Despite its seemingly confusing name, it does not measure serum T3 levels but uses a radioactive isotope of this hormone to determine unbound (unsaturated) TBG. The test is performed by adding a given amount of radioactive T3 to a system containing an aliquot of the patient's serum and an anion exchange resin impregnated sponge. Depending upon how saturated the patient's TBG is with endogenous thyroxine, the added radioactive T3 hormone will either bind to the TBG or to the resin sponge. Thyrotoxic serum has a relatively normal amount of TBG but it is highly saturated with T4. Thus, this serum has only a small number of TBG binding sites to accommodate the added radioactive T3 (which like T4, binds to TBG) and a high resin uptake is obtained. Conversely, hypothyroid serum has essentially normal amounts of circulating TBG but virtually no endogenous thyroxine to occupy these sites. Hence, the high degree of avidity of this TBG to exogenously added radioactive T3 results in only a small amount bound to the resin and hence a low resin uptake. Because the RT3 uptake test is an inverse function of unsaturated ("free") TBG, factors which alter TBG without affecting free hormonal levels alter the RT3 determination in an inverse manner to that of the T4D. This is expressed by the mathematical relationship:

$$\text{RT3} = K_1\text{x}[\text{TBG}]^{-1} \quad \ldots\ldots\ldots\ldots\ldots 4$$

Hence, estrogens, by increasing unbound as well as bound TBG, are reflected by lower RT3 values but higher T4D levels; contrariwise, androgens raise the RT3 values but lower the T4D levels for analogous reasons. As theoretically anticipated by formula 3 above and as proved by many clinical reports, the product of these two factors provides essentially the same measure of FT4 as by dialysis tests but by more available means.

As the RT3 uptake test is readily performed in most clinical laboratories, as is the T4D determination, the

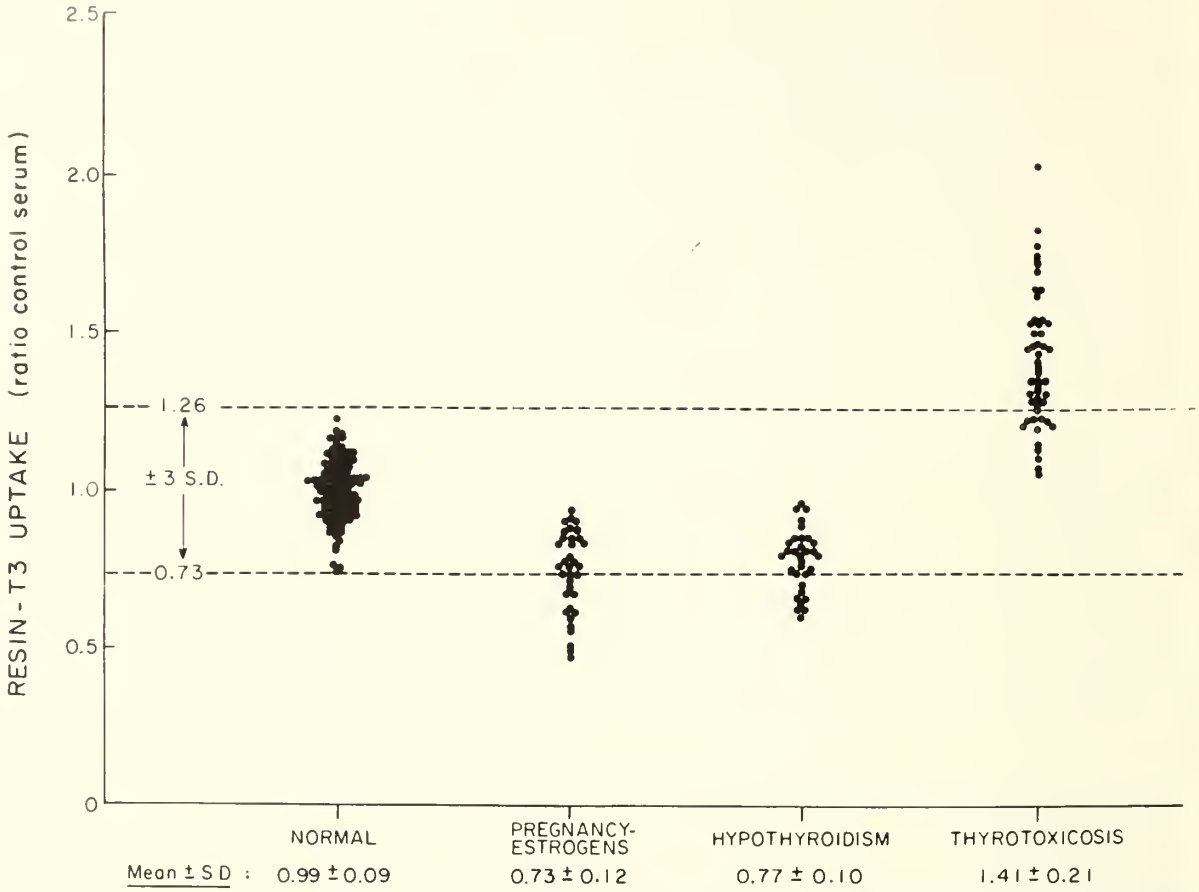

Fig. 8. Values for the resin-T3 uptake ratio (RT3) by the resin sponge method (Triosorb®, Abbott) in normal subjects and in patients on estrogens or pregnant, hypothyroidism or hyperthyroidism obtained in the Thyroid Laboratory at the Peter Bent Brigham Hospital.

product obtained by multiplication of these values (FTI-T3) provides the most expedient, accurate and relevant way of estimating serum free thyroxine levels (Fig. 9). It is useful, and rapidly being accepted as a convention, that the RT3 uptake be expressed as a *ratio* of a standard reference serum. Thus, since the experimental uptake range for the resin sponge method is generally given as 25-35%, and since a mean value in most laboratories for the standard reference serum is about 30%, the RT3 *ratio* for the normal range is 25%/30% to 35%/30% or 0.83 to 1.17. Values for the RT3 ratio and the derived FTI-T3 obtained in this laboratory for normal subjects and patients with common thyroid disorders are shown in Figs. 8 and 9. Clinically useful ranges for the T4D, RT3 ratio and FTI-T3 derived from frequency distribution data in our laboratory are given in Table 2.

We have recently developed a variant of the resin-T3 uptake test. Rather than employ T3 as the radioactive hormone, we now use T4 and hence, perform a resin-T4 (RT4) uptake test. This is particularly advantageous because the same system and the same isotopic T4 used for determination of the T4D can also be used in the RT4 uptake test. Like the RT3, the RT4 is also expressed as a *ratio* of a standard reference serum. The FTI obtained by the mathematic product of these two factors (FTI-T4) has been shown to provide a more distinct separation of euthyroid values from those in hyperthyroidism and hypothyroidism than the FTI obtained utilizing the RT3 uptake (FTI-T3). The useful clinical diagnostic ranges of the T4D, RT4 and FTI-T4 are given in Table 3. It will be noted that the RT3 or RT4 uptakes, when expressed as a ratio of a standard reference serum, apply a correction to the T4D to allow for changes in that parameter produced by changes in serum TBG levels. The free thyroxine index is probably the most useful parameter of the thyrometabolic state currently available.

The final category of thyroid function tests relates to measurements of tissue metabolic functions (Fig. 1 and Table 1). It is not relevant to enumerate here all the peripheral effects of thyroid hormones. Suffice it to say that because of the many non-specific actions of thyroid hormones on cellular systems and because of the propensity of other hormones, physiologic states and pharmacologic agents to produce similar effects, tests that measure these peripheral actions are generally relatively imprecise, non-specific and subject to a wide variety of

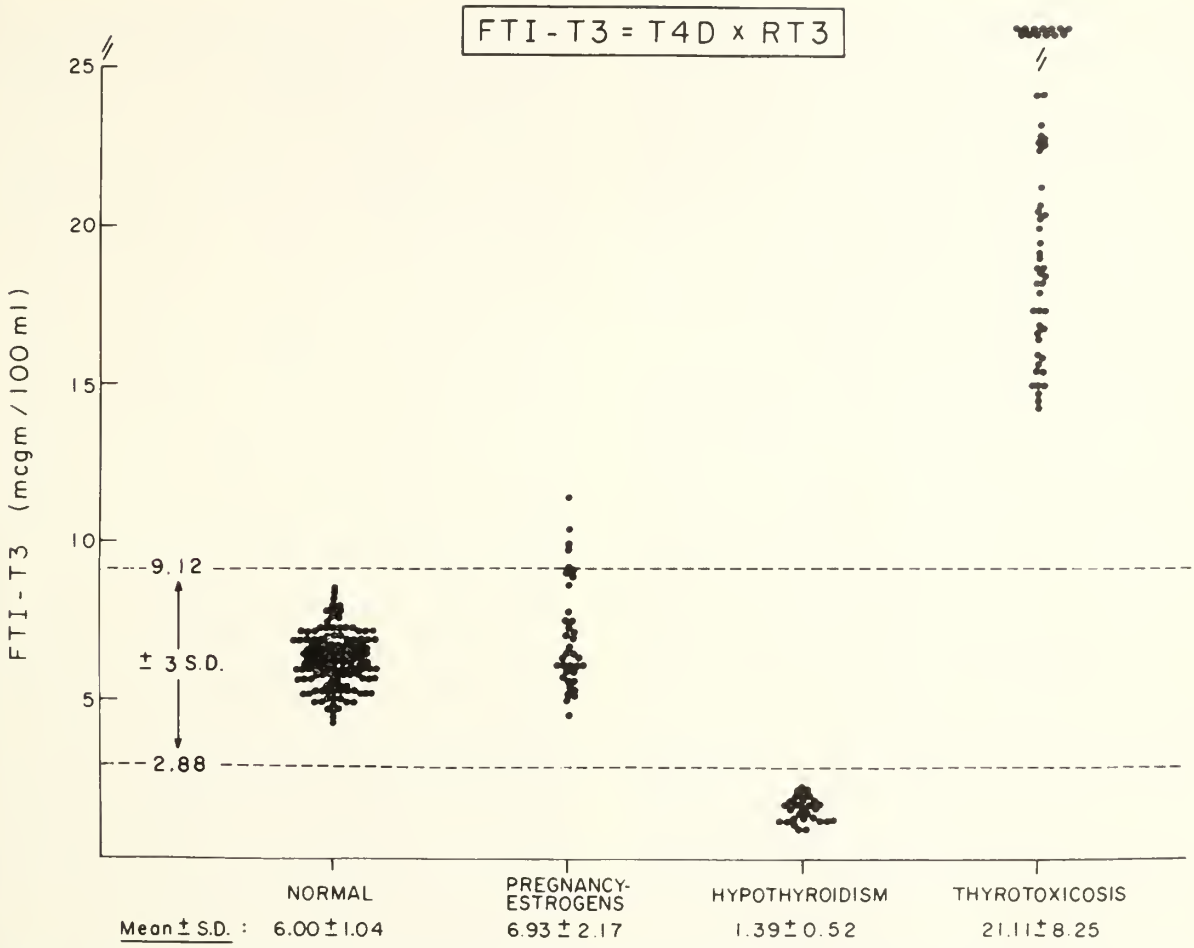

Fig. 9. Values for the FTI-T3 in normal subjects and in patients on estrogens or pregnant, hypothyroidism or hyperthyroidism obtained in the Thyroid Laboratory at the Peter Bent Brigham Hospital.

TABLE 3

CLINICALLY USEFUL RANGES FOR T4D, RESIN-T4 RATIO (RT4) AND FTI-T4 DERIVED FROM FREQUENCY DISTRIBUTION DATA OBTAINED IN THE THYROID LABORATORY, PETER BENT BRIGHAM HOSPITAL

Diagnostic Category	*T4D μg/100 ml*	*RT4 Ratio*	*FTI-T4*
Hypothyroid	<3	0.5 - 0.7	<3.5
Borderline Low	3-4	0.7 - 0.8	3.5 - 4
Euthyroid	4-10	0.8 - 1.30	4 - 10.5
Borderline High	10-12	1.30 - 1.40	10.5 - 13
Hyperthyroid	>12	>1.40	>13

errors of commission or omission. The basal metabolic rate (BMR) was one of the first available laboratory tests of thyroid function. This oxygen determination is increased in hyperthyroidism and decreased in hypothyroidism. As it is a measure of total basal oxygen consumption, the BMR in states such as anxiety, pregnancy, fever, etc. can be elevated while a wide variety of conditions ranging from obesity to narcolepsy can diminish the BMR values. Although usually elevated in hyperthyroidism and decreased in hypothyroidism, is not generally helpful diagnostically since it is affected by so many other medical conditions.

The relaxation phase of the deep tendon reflexes are exaggerated in hyperthyroidism and depressed in hypothyroidism. This manifestation of thyroid function can be recorded by one of several varieties of electrical devices sold commercially. Unfortunately, quantification of this reflex is imprecise and results are often misleading, particularly in the diagnosis of hyperthyroidism. The results of these and a variety of other tests that presumably measure peripheral actions of thyroid hormones should only be treated as adjunctive tests of thyroid function. While of some utility and interest, diagnoses should neither be ruled in or out on the basis of these tests.

THE THYROTOXIC STATE

Thyrotoxicosis with its protean clinical manifestations is one of the few endocrine disorders which can be ameliorated or even cured by rather simple and readily available therapeutic means. It is, indeed, a rewarding moment for the physician when he recognizes the cause of atrial fibrillation and congestive heart failure to be a

cryptic or "masked" form of hyperthyroidism – so-called thyrocardiac disease. With the obvious importance of diagnosis kept constantly in mind, let us now review briefly the etiologies, clinical manifestations and therapeutic modalities for this common endocrinopathy. For more complete discussions of this important subject, the reader is referred to more rigorous reviews. The present comments are intended mainly to emphasize important aspects of the general problem and to relate these to daily medical practice. The complete restoration of the thyrotoxic patient should be within the therapeutic capabilities of all practicing physicians.

The terms thyrotoxicosis and hyperthyroidism are often used interchangeably both here and elsewhere. But in the strict sense, *hyperthyroidism* implies hyperfunctioning of the thyroid gland with or without an excessive production of thyroid hormones, while *thyrotoxicosis* refers to that disease state secondary to tissue actions of excessive thyroid hormones. Autonomous hyperfunctioning of the thyroid gland is the hallmark of hyperthyroidism. Excessive tissue metabolic rates associated with increased levels of free thyroid hormones is characteristic of thyrotoxicosis. Hyperthyroidism can exist without thyrotoxicosis; and conversely, thyrotoxicosis can exist without hyperthyroidism.

Although there are several etiologies of the thyrotoxic state, the two of greatest clinical significance are associated either with the so-called long acting thyroid stimulator (LATS) or the disease state caused by autonomous hyperfunction of portions of the gland itself. The latter may be mediated through autonomous hyperfunction of a single "hot" nodule or a summation of several autonomous nodules as in thyrotoxicosis due to multinodular goiter (Plummer's disease). The former, often called Graves' disease, includes the triad of goiter, exophthalmos and hyperthyroidism. It is the exophthalmos, as well as the less commonly associated pretibial myxedema, that distinguish this variant of the thyrotoxic state from all others. The extra-thyroidal and systemic manifestations of Graves' disease have no direct relationship to the degree of thyroidal hyperfunction. Similarly, treatment of the overactive thyroid gland has no direct bearing on their amelioration or clinical course. The exophthalmos, pretibial myxedema, acropachy, splenomegaly and other systemic phenomena are probably related to the presumed auto-immune nature of this disorder rather than to thyrotoxicosis. The degree of exophthalmos may lessen, increase, or remain unchanged following therapy in a hyperthyroid individual but no accurate prediction of the course of this affliction can be made prior to treatment. Graves' disease affects women more often than men (at least 5:1 in our experience), is most common in the middle age groups (20-40 years) and is associated with metabolic manifestations to a greater extent than thyrocardiac or thyromyopathic symptomatology.

The thyrotoxic state secondary to autonomous thyroid nodules, on the other hand, while still affecting females to a greater extent than males, is a disease of the older age groups. It is often associated with myopathic and cardiac symptomatology. Therefore it is not only imperative that it be treated efficaciously but it is more important that this diagnosis be suspected whenever obscure cardiomyopathies occur. The latter statement is emphasized by consideration of several important observations. It is not uncommon for the physician to deal with a high proportion of cardiac patients, many of whom have atrial fibrillation. Second, cardiac manifestations, are often so outstanding that even in the presence of other clinical manifestations, treatment of the heart disease is often foremost in the mind of the attending physician. Third, exophthalmos and pretibial myxedema are usually not present in this type of thyrotoxicosis although a stare and lid lag may be present. Fourth, as opposed to Graves' disease in which the thyroid gland is diffusely enlarged and readily palpable, a nodular goiter can often be missed on casual examination, particularly since the thyroid is not uncommonly substernal in elderly subjects and therefore inaccessible to routine palpation. Fifth, even if metabolic symptoms are present, they can be obscured by a variety of geriatrically related dysfunctions. For example, the hyperdefecation of thyrotoxicosis can be "neutralized" by the usual constipation following middle age; the expected warm extremities may be offset by some degree of peripheral vascular insufficiency; and the tremor found in the thyrotoxic state is also found to some extent in man elderly patients. Finally, laboratory tests are often borderline in thyrocardiac patients, probably because of myopathic effects of a small excess of circulating thyroid hormones present over a prolonged period in this age group. Unfortunately, a thyroid suppression test is often contraindicated in these patients when they already manifest overt cardiac symptoms. The addition of 100 mcgm of T3 (liothyronine, Cytomel) per day for a week might be the metabolic "straw that broke the back" of a minimally compensated cardiovascular system. Thus, one is sometimes relegated to the uncomfortable task of having to rely solely on clinical judgement. Under many such circumstances, the physician's cautious appraisal of a thorough history and a careful physicial examination will be rewarded by an almost miraculous therapeutic result. When this latter fails to occur, the physician must "back off" and take another look.

Listed in Table 4 are some clinical paradoxes helpful in diagnosising the obscure aspects of thyrocardiac disease.

Other extremely rare causes of the thyrotoxic state are metastic thyroid carcinoma, ectopic TSH producing tumors (classically choriocarcinoma, although this phenomenon has been described with other varieties of neoplasms) and theoretically, non-suppressible struma ovarii found in ovarian teratomata. A slightly more common etiology than the above is thyrotoxicosis factitia, where the affected individual willingly takes or is given (e.g., by "diet" or "obesity" specialists) large quantities of

TABLE 4

CLINICAL PARADOXES SUGGESTING THYROCARDIAC DISEASE

Weight Loss	despite	Good Appetite
Rapid Atrial Fibrillation	despite	Digitalis Therapy
Minimal Congestive Heart Failure	despite	Marked Cardiac Signs
Shortened Circulation Time	despite	Heart Failure
Striking Myopathy	despite	Recent Heart Disease
Stable Heart Disease	despite	Excessive Physical Activity

exogenous thyroid hormones. The ingested quantity, indeed, must be rather inordinately high because it requires the equivalent of at least 10 or 15 grains of desiccated thyroid daily to render human subjects clinically symptomatic. This diagnosis of thyrotoxicosis is commonly made by demonstrating an elevated free thyroxine index (FTI-T3 or FTI-T4) in the presence of a very *low* radioactive iodine uptake. In the rarer forms of thyrotoxicosis factitia in which the individual ingests large amounts of T3 (liothyronine, Cytomel), the FTI is low rather than high. This is because the T4D does not ordinarily measure T3 and is thus very low in patients receiving this hormone. The RT3 or RT4, the other parameter necessary to calculate the FTI, is normal in this disorder. These facts in concert with a careful history (often one containing some degree of psychopathology) and physical examination (absence of an enlarged thyroid gland or thyroid nodules) helps confirm the diagnosis of factitious thyrotoxicosis.

As thyroxine is a non-specific general mediator of bodily metabolic functions, it seems logical that all organ systems are affected when there is an excess of this hormone. The integument becomes smooth, moist and warm. Pruritus is a not uncommon complaint in the absence of any rash. Hair is fine, tends to lose any natural curling ability and a small degree of temporal baldness may be present. The nail plate becomes separated from the nail bed, a phenomenon known as onycholysis (Plummer's nails) and this is seen most commonly, for unknown reasons, in the fourth digit of each hand. Bones may become osteoporotic and this phenomena is responsible for the hypercalciuria and (less commonly) hypercalcemia found in thyrotoxicosis. Myopathies are a frequent finding, particularly in the proximal limbs, and in muscles of ocular movement. Despite an increased appetite, weight loss is common as is hyperdefecation. Rarely, there may be anorexia and/or weight gain. Tachycardia and associated arrhythmias are usually present, the most common of the latter being paroxysmal or constant atrial fibrillation. These are usually somewhat refractory to the usual doses of cardiac glycosides. CNS stimulation is common with concomitant nervousness, irritability and emotional lability. A fine tremor and hyperkinetic deep tendon reflexes are usually present. Lymphadenopathy (very rarely palpable splenomegaly) with accompanying relative lymphocytosis on blood smear occurs commonly. Accompanying endocrinopathies include glucose intolerance, diminished adrenocortical "reserve," increased sensitivity to catecholamines, hypo and oligomenorrhea in the female and diminished libido and impotence in the male.

The diagnosis of hyperthyroidism is made best on clinical grounds. It is confirmed by demonstrating elevated circulating hormone levels (PBI, T4D), elevated resin uptake values (RT3, RT4) and, hence, an elevated free thyroxine index (FTI-T3). In states associated with elevated thyroxine binding proteins (pregnancy, estrogens), the PBI or T4D which is elevated under such circumstances in the euthyroid state, becomes even more elevated with associated thyrotoxicosis (PBI values of 15-20 mcg% and T4D values of 20-25 mcg% are not rare). The RT3 and RT4, which are low in an euthyroid individual with TBG excess, become normal when this subject is thyrotoxic. The net effect of thyrotoxicosis and estrogens (or pregnancy) is to render the FTI elevated. This now becomes diagnostically meaningful because the FTI is a reflection of the "free" or metabolically significant portion of circulating thyroxine. On the other hand, in a thyrotoxic individual with TBG deficiency (androgens, chronic illness), the converse is true with a resultant increased FTI value (FTI-T3). Other useful laboratory results in hyperthyroidism include an elevated RaI uptake and a thyroid scan showing either diffuse hyperplasia (Graves' disease) or one or more hyperfunctioning nodules (Plummer's disease). Hypocholesterolemia, tyrosine intolerance, hypercalciuria, creatinuria and (rarely) hypercalcemia are associated laboratory findings. Serum enzyme levels are usually low.

There are presently three distinct modalities for treatment of the thyrotoxic state. Despite this, there are rather clear lines of delineation for selecting the appropriate form of therapy suited best to the individual patient. The three modalities are: a) antithyroid drugs; b) subtotal thyroidectomy; and c) radioactive iodine. This list excludes a fourth modality, namely stable iodine. This particular agent *alone* has no place as a primary therapeutic agent, although it is of ancillary importance when used in concert with other methods.

It is difficult for many physicians to understand how stable iodine, which is so vital to the normal physiology of the thyroid gland, also inhibits the production and release of thyroid hormones. Nonetheless, this occurs by two distinct mechanisms: firstly, by inhibition of proteolysis of thyroglobulin, thus decreasing release of thyroid hormones; and secondly, by inhibition of synthesis of thyroxine and triiodothyronine (Wolff-Chaikoff effect) in a manner similar to the antithyroid drugs. Iodine, in small pharmacologic doses, has these distinct effects. A third action, that of diminution of thyroidal vascularity, is particularly important in rendering the thyroid gland suitable for surgical excision. Iodine is thus a necessary agent for preoperative preparation of the thyrotoxic patient. In fact, when Henry Plummer, in 1923, re-introduced iodine as a necessary pre-operative measure in thyrotoxicosis, thyroid surgical morbidity and mortality was reduced significantly – the first major

therapeutic advancement in the treatment of thyrotoxicosis.

Introduction of the antithyroid drugs into clinical therapy by Astwood in 1946 represented a second major breakthrough. From a conceptual viewpoint, antithyroid drug therapy represents the most physiologic approach to the therapy of the thyrotoxic state since it is the only modality which permits the natural occurrence of a spontaneous remission. Ablative therapy, either isotopic or surgical, permanently destroys portions of all abnormal thyroid tissue whereas induction of a spontaneous remission by antithyroid drugs preserves the integrity of the gland. Antithyroid treatment is generally selected for the majority of thyrotoxic individuals who are too young to be given radioactive iodine. It is generally considered the first approach to therapy prior to consideration of a surgical procedure. Indeed, all patients seen in our clinic who are under the age of thirty-five, unless medically unreliable or proved to have allergic or idiosyncratic reactions, are started on a program of antithyroid drugs with the later addition of replacement dose of thyroid hormones. For this purpose we usually use either propylthiouracil (PTU) or methimazole (Tapazole®) in daily divided doses of 300 mg. of the former or 30 mg. of the latter. When the patient becomes euthyroid on antithyroid drugs, full replacement doses of thyroid hormones are then added. All pregnant thyrotoxic women, unless specific contraindications exist, are treated by such a combined antithyroid-thyroid program.

Unfortunately, antithyroid drugs, although effective in preventing synthesis of thyroid hormones, in many instances control rather than cure the thyrotoxic state. Unless these drugs are taken every six or eight hours on a regular daily basis, the underlying disease may often exacerbate. In fact, it is only because Graves' disease is a self-limiting entity that antithyroid drug therapy is truly "therapeutic." These drugs probably act by maintaining an euthyroid state long enough for the individual to go into spontaneous remission. For this reason, not only is the thyrotoxic state associated with multinodular goiter usually not effectively remedied by these agents, but also the extrathyroidal concomitants of Graves' disease (namely exophthalmos and pretibial myxedema) are also not predictably altered directly by this therapy. Nonetheless, of all presently available modalities of therapy, these drugs appear to be the least likely agents to aggravate pre-existing thyrogenic ophthalmopathy. Major side-effects of the antithyroid drugs are blood dyscrasias (namely granulocytopenia and rarely, agranulocytosis) and skin rashes of all varieties. The latter can often be remedied by lowering the dosage or, at times, by addition of an antihistamine drug; the former, while rare, require changing to a totally different therapeutic approach. It is of little value to get regular white blood cell counts in anticipation of granulocytopenia or agranulocytosis, any more than a routine EKG could always predict that a patient would subsequently have a massive myocardial infarction. An initial WBC count, however, does provide a useful baseline for later comparisons and should be obtained. More importantly, the patient on antithyroid drugs should be alerted to signs and symptoms that may be associated with the leukopenic state.

The usual starting dosage of propylthiouracil is 200 to 400 mg. and Tapazole 20 to 40 mg. per day in 3 to 4 divided doses. On rare occasions, higher dosages may be required. The minimal dosage most effective in maintaining euthyroidism should be used after adequate control is attained. We routinely add supplementary thyroid in physiologic replacement doses for all patients once euthyroidism is achieved. This is especially indicated in pregnant women with thyrotoxicosis. It prevents hypothyroidism which may occur as a result of the unopposed actions of antithyroid drugs in pregnant thyrotoxic women. Another advantage of using thyroid along with an antithyroid program is that we have a "built-in" thyroid suppression test. The patient is continued on thyroid hormones even after the antithyroid drug is discontinued at the end of a therapeutic course. Thus, if the RaI uptake remains elevated while the patient is taking full suppressive doses of thyroid hormones, the chances are high that a recurrence of thyrotoxicosis will occur in the imminent future. On the other hand, if the 24-hour RaI uptake is suppressed (generally below 20% in 24 hours) this signifies a spontaneous remission and a good prognosis for prolonged euthyroidism.

The incidence of spontaneous remission following a year or more of a well applied course of an antithyroid drug varies between 40-60 percent depending upon the design and execution of the experimental series. In general, if the course of therapy is successfully completed and a remission follows, no further therapy is required. This occurs most often in patients with relatively small goiters at the outset and under conditions when the goiter size remains steady or decreases with time. If there is a therapeutic failure or if a remission does not occur spontaneously, one of three choices are then open: a repeat, prolonged course of antithyroid drugs; subtotal thyroidectomy; or, therapeutic radioactive iodine. Selection of the appropriate course depends upon the patient's age, circumstances and willingness to cooperate, among other factors. This selection, after one antithyroid drug failure, should be "tailored" to suit the needs and circumstances of the patient. Of the three choices, therapeutic radioiodine is the least expensive and most easily administered. However, if the patient is under 35 years of age, or if there is active suffusive ophthalmopathy present, we prefer either a second course of medical therapy or subtotal thyroidectomy.

Subtotal thyroidectomy has been used successfully for correction of thyrotoxicosis for many years. It is an ablative form of therapy and thus does not carry the benefit of inducing a spontaneous remission as does antithyroid drug therapy. At present, it is usually reserved for the following patients. First, those who have failed to achieve a spontaneous remission after one or more ade-

quate courses of antithyroid drugs and who are not candidates for radioactive iodine therapy. Secondly, the rare patient who cannot be controlled by even relatively large doses of antithyroid drugs or who has developed serious reactions to them. And thirdly, those patients, who, for whatever legitimate reasons, cannot be entrusted to medical therapy (psychotic patients, psychopathic persons, socially maladjusted patients, etc.). Generally speaking, recurrent thyrotoxicosis in patients previously treated by subtotal thyroidectomy is an indication for radioactive iodine; this is indicated even in the young after surgical thyroidectomy. The reason for this is because any potential hazzard of radioactive iodine therapy is usually outweighed by the increased risks of a *second* subtotal thyroidectomy.

Multinodular goiter and "hot" thyroid nodules with thyrotoxicosis may not respond satisfactorily to either antithyroid drugs or radioactive iodine therapy. If so, subtotal thyroidectomy or excision of the single "hot" nodule is indicated. In general, patients in whom surgical thyroid excision is indicated for thyrotoxicosis should be properly prepared pre-operatively so that the surgical procedure is no more taxing to the patient than subtotal thyroidectomy for non-toxic goiter. Under no circumstances should an ill-prepared patient be permitted to undergo this operation since the risks increase significantly if thyrotoxicosis persists. All patients should be given iodide therapy (usually a saturated solution of potassium iodide 5 drops thrice daily) for 10 days prior to operation. The antithyroid-thyroid therapy should be continued to the day of operation. If any doubt exists as to whether full euthyroidism has been achieved prior to operation the procedure should be delayed. Clinical findings such as a normal ($\pm$ 80/minute) resting pulse and absence of tremor are reassuring. A serum T4D and RT3 (and thus a normal FTI-T3) are useful confirmatory laboratory tests which are not interfered with by the presence of even large quantities of serum iodide. If all appropriate pre-operative measures are taken and the patient is fully euthyroid at the time of operation, the risks of this procedure are minimal and the outcome generally is quite satisfactory.

The foremost and theoretically most ideal agent for treatment of the thyrotoxic state is radioactive iodine. In view of the high predelection of the thyroid gland for iodine, radioactive iodine (^{131}I) provides a most efficacious and relatively innocuous mode of therapy. It is, in reality, a non-surgical thyroidectomy! Unfortunately, there are several reservations to its use in the treatment of the thyrotoxic state. Foremost is the fact that it is a form of radiation therapy. Despite the fact that in the generation that it has been in use no single case of thyroid cancer or significant genetic damage has been proved to be related to its radiation effects, it is still too early to feel dogmatically secure. Despite the relatively small amount of total body radiation from a therapeutic "cocktail," chromosomal aberrations have been reported in peripheral leukocytes following its use. For this reason, and with little exception, we reserve use of this agent for patients over 35 years of age and for women who do not wish to, or who are unable to bear more children. This last fact presents somewhat of a therapeutic problem because Graves' disease is statistically more prevalent in younger patients and it is this group which is most likely to respond to radioactive iodine therapy because of their diffuse rather than multinodular goiters.

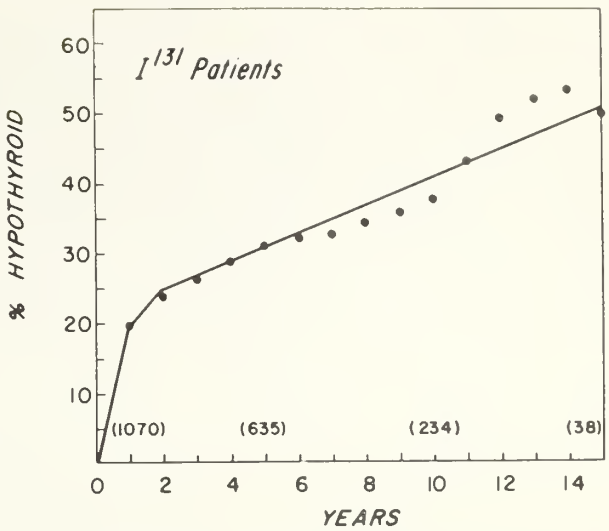

Fig. 10. Cumulative incidence of hypothyroidism following therapeutic radioactive iodine for thyrotoxicosis. (Dunn, J. T. and Chapman, E. M., New Eng. J. Med. *271*: 1037, 1964).

If a patient does not respond to the initial therapeutic dose, the second dose of radioactivity required is generally larger than the first. This is necessary not merely for the obvious reason that the first dose was not sufficient, but because the radiation effect from the first treatment renders the gland relatively more insensitive and thus a greater amount of radioactivity is necessary to accomplish the requisite effect. The complications of ^{131}I therapy are generally insignificant except for one – post-radiation hypothyroidism. This occurrence is not merely an acute phenomenon. After an average therapeutic dose, hypothyroidism results with an incidence of about three percent a year after the first year (Fig. 10). This means that over half the patients treated with radioactive iodine will become hypothyroid within a period of about 15 years. Nonetheless, this consequence can be readily anticipated and remedied. To prevent post-radioiodine hypothyroidism, it is our policy to place all patients who have received therapeutic amounts of radioactive iodine for thyrotoxicosis on thyroid hormone replacement. This is done irrespective of whether or not they are hypothyroid at that time. Such prophylactic therapy is inexpensive, readily accepted by patients and certainly prevents those who may be lost to follow-up, from insidious development of thyroid failure. It has the added advantage of being beneficial in preventing

Continued on Page 214

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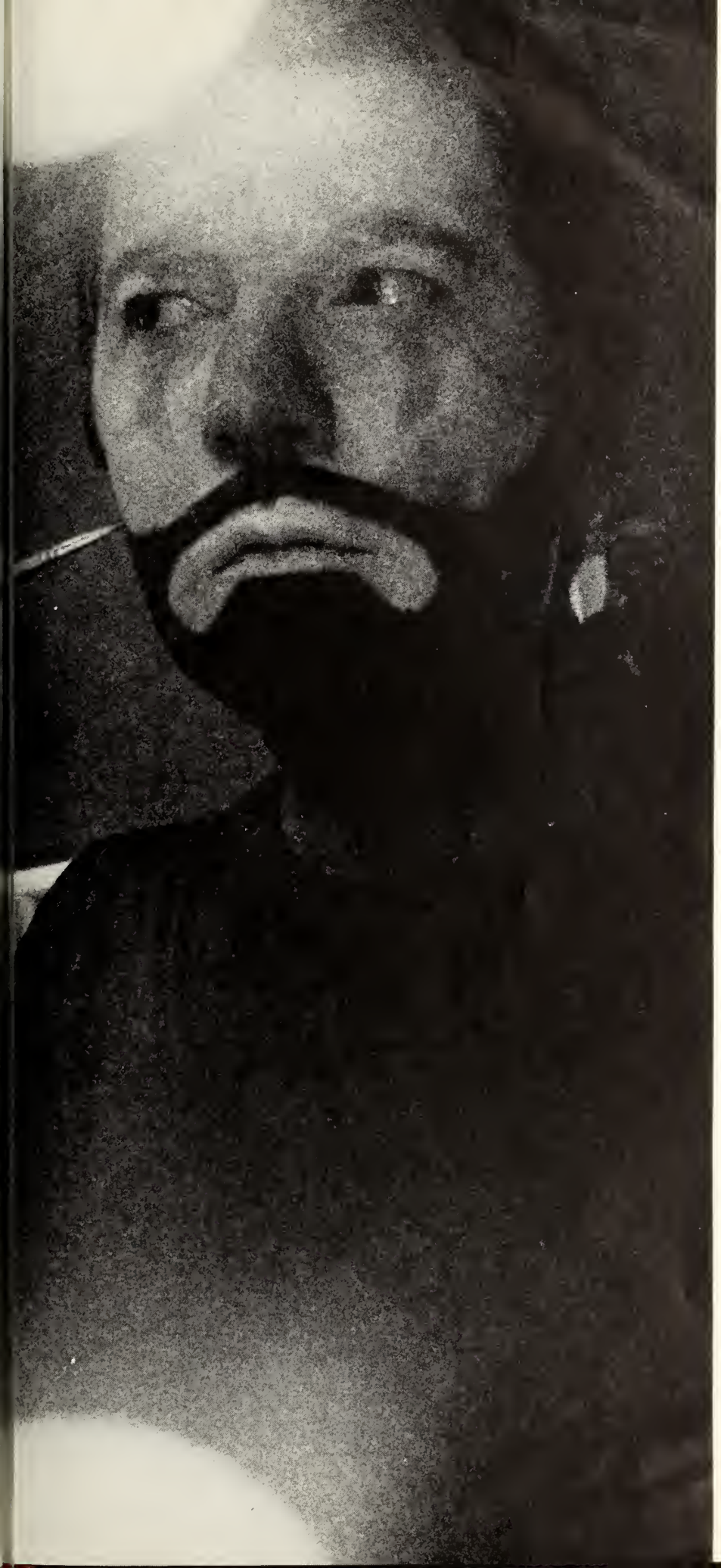

Pro·Banthine®
(propantheline bromide)

Indications: Peptic ulcer, gastroenteritis, pylorospasm, biliary dyskinesia, functional hypermotility and irritable colon.

Contraindications: Glaucoma, severe cardiac disease.

Precautions: Since varying degrees of urinary hesitancy may occur in elderly men with prostatic hypertrophy, this should be watched for in such patients until they have gained some experience with the drug. Although never reported, theoretically a curare-like action may occur with possible loss of voluntary muscle control. Such patients should receive prompt and continuing artificial respiration until the drug effect has been exhausted.

Side Effects: The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.

Dosage: The maximal tolerated dosage is usually the most effective. For most adult patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily may be required. Pro-Banthine is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg. The parenteral dose should be adjusted to the patient's requirement and may be up to 30 mg. or more every six hours, intramuscularly or intravenously.

Pro-Banthine® 15 mg.
(propantheline bromide)
with
Dartal® 5 mg.
(thiopropazate dihydrochloride)

Indications: Peptic ulcer, spastic constipation, nonspecific gastritis, functional gastrointestinal disorders, pylorospasm, hyperhidrosis, irritable bowel syndrome, mucous or ulcerative colitis, functional diarrhea.

Contraindications: Glaucoma, severe cardiac disease.

Warnings: Pro-Banthine with Dartal should not be administered to patients who are under the influence of barbiturates, alcohol or narcotics. The drug should be administered cautiously to epileptic patients or those in depressed states, patients with liver disease and to pregnant women. Hypersensitivity to Dartal may occur rarely in patients with known sensitivity to similar drugs.

Side Effects: Dryness of the mouth, mydriasis, hesitancy of urination; less commonly extrapyramidal (restlessness, dystonia and signs of pseudoparkinsonism such as muscular rigidity, fixed facies, tremor, ataxia, festinant gait and drooling), parasympatholytic (blurred vision, xerostomia, hypotension, nasal congestion and constipation) and curare-like (loss of control of voluntary muscles, particularly the muscles of respiration) reactions. Rarely, leukopenia or allergic purpura. A generalized erythematous skin reaction may occur. Side effects characteristic of phenothiazines such as grand mal convulsions, altered cerebrospinal proteins, cerebral edema, potentiation of the effects of atropine, heat or phosphorus insecticides, autonomic reactions, endocrine disturbances, reversed epinephrine effect, hyperpyrexia or pigmentary retinopathy may theoretically occur but have not been reported with Dartal. Severe hypotension following recommended doses occurs more commonly in patients who are also afflicted by other medical disorders such as mitral insufficiency or pheochromocytoma, and particular attention should be paid to such a possibility although this has not been observed with Dartal.

Adult Dosage: One tablet three times a day.

Pro-Banthine® 15 mg.
(propantheline bromide)
with
Phenobarbital 15 mg.

Warning: May be habit-forming.

For *Indications, Contraindications, Precautions, Side Effects* and *Dosage* see Pro-Banthine. In addition, phenobarbital should be administered with caution to patients with liver disease, mental disturbances or a significant degree of hypoxia.

Pro-Banthine P.A.®
prolonged acting brand of propantheline bromide

For *Indications, Contraindications, Precautions* and *Side Effects* see Pro-Banthine.

Dosage Form: Capsule-shaped, compression-coated, peach tablets of 30 mg. for oral use.

Dosage: The recommended initial dosage is one tablet in the morning and one at night.

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the undesirable effects of hypothyroidism on an existing suffusive ophthalmopathy.

The initial dosage of ^{131}I is approximately 4-8 mCi for diffuse hyperplasia and 8-15 mCi for multinodular hyperfunctioning goiters. All treated patients are given a saturated solution of potassium iodide (SSKI), 5 drops q.d., starting three days after the therapy and continued for a total of three weeks. This is advised for several distinct reasons: a) iodide acts directly by blocking the proteolytic phase and the release of thyroid hormones from the gland; and thus, the patient (particularly the elderly thyrocardiac) has a more immediate amelioration of symptomatology than is achieved by waiting the four or more weeks for the radioactive destruction to take effect; and b) this phenomenon augments retention of the radioactivity by the thyroid gland by retarding release of newly synthesized radioactive thyroid hormones. This latter action of iodide permits a full therapeutic effect to be delivered to the thyroid gland by a lower dosage of ^{131}I, thus reducing the total body radiation burden. Once euthyroidism is achieved by this means, replacement therapy with thyroid hormones is begun and the patient is advised to continue this therapy *for life.*

Our indications for use of radioactive iodine can be stated generally as follows: a) all patients beyond the active child-bearing age (usually over 35 years); b) most patients at any age who have undergone previous subtotal thyroidectomy for thyrotoxicosis and have a recurrence; c) patients at any age beyond 20 years who are sterile, have serious complicating systemic diseases (diabetes, rheumatic heart disease, active tuberculosis, psychoses, etc.) or who for some reasons are unable to take antithyroid compounds (toxicity) or are not a good operative risk. Therapeutic radioiodine is not usually given below adulthood and under no circumstances should a therapeutic dose of radioactive iodine be given during pregnancy. Occasionally, patients may fail to respond to even large doses of radioactive iodine. This is rare but it usually occurs in patients with large, nodular goiters and thyrotoxicosis (Plummer's disease). Under such circumstances, subtotal thyroidectomy may be indicated since antithyroid drugs generally are also not particularly efficacious. In the future, if the potential undesirable radiation effects of radioactive iodine do not occur, it may become the therapy of choice for all patients regardless of age. Use of replacement therapy with thyroid hormone preparations will be discussed in the section on therapy of hypothyroidism.

The Hypothyroid State

We next turn to the hypothyroid or thyroprivic state. The clinical manifestations of total lack of thyroid hormone activity are in diametric contrast to those of thyrotoxicosis. Because of the general bodily dependence on this hormone for a variety of functions, its absence produces symptomatology related to practically all organ systems. The term myxedema is frequently used interchangeably with hypothyroidism. In more exact terminology, however, myxedema denotes only that severe thyroprivic state in which a mucinous polysaccharide infiltrate becomes clinically prominent in conspicuous tissues. In general, it represents the extreme, chronic form of total thyroid hormone deprivation.

For all practical purposes, there are two major etiologies of hypothyroidism: primary and secondary (pituitary). The former includes not only the disease states associated with primary destruction of the thyroid gland (whether idiopathic or iatrogenic) but also that secondary to inborn errors of thyroid metabolism. At present, iatrogenic causes of hypothyroidism related to ablative treatment of hyperthyroidism with radioactive iodine or subtotal thyroidectomy are the most common. The idiopathic variety is probably related to an autoimmune phenomena generally known as Hashimoto's Struma. Support for this etiology is given by the following observations: a) the occurrence of serum thyroglobulin antibodies in high titers in such affected persons as opposed to its virtual absence in hypothyroidism of other etiologies (e.g., secondary to ^{131}I); b) the association of primary hypothyroidism with other of the so-called autoimmune disease states (e.g. rheumatoid arthritis, disseminated L.E., pernicious anemia); and c) the histologic appearance of these thyroid glands showing remnants of parenchyma surrounded by large clusters of lymphocytes and plasma cells.

Pituitary myxedema, while much rarer, is quite important to diagnose correctly and to treat early for a variety of reasons. On one hand, it is important to ascertain as soon as possible the specific etiology of the pituitary insufficiency. In this way, there may be hope for treatment of an underlying tumor (e.g., chromophobe adenoma) or granulomatoma process (e.g., tbc or sarcoidosis). Second, correction of other trophic hormone insufficiencies by target hormone replacement therapy (e.g., corticosteroids and sex hormones for ACTH and gonadotrophin replenishment, respectively) is important for total restoration of the affected patient to an adequate state of health. Third, and most critical, giving thyroid hormones to a partially decompensated hypopituitary individual could precipitate an Addisonian crisis. This occurs because the hypothyroid state is associated with a reduced need for target hormones, particularly glucocorticoids. Thus, diminished target hormonal levels are tolerated while the hypothyroid state exists. However, when thyroid therapy is instituted, the cellular *need* for glucocorticoids is increased but not satisfied due to lack of pituitary ACTH. Adenocortical crisis can thus be induced iatrogenically! It is vital to start adrenocortical replacement prior to thyroid therapy in the treatment of pituitary myxedema.

Aside from the manifestations secondary to lack of circulating thyroid hormones, there are two particular clues one can look for in the routine history and physical examination of an individual suspected of pituitary insufficiency. The first deals with etiology. The astute

physician should be cognizant of neurologic and visual field disturbances associated with pituitary tumors or vascular diseases. A history of head trauma, for example, or a recent pregnancy with post-partum hemorrhage are important to elicit. Likewise, questions related to tuberculosis or sarcoidosis (constitutional symptoms, cough, skin lesions) or other granulomata (e.g., eosinophilic granuloma) should be asked. The second aspect deals with the symptoms produced by lack of other pituitary hormones, including gonadotropins, ACTH and pitressin. These include amenorrhea, impotence, loss of pubic and axillary hair, decreased libido, lightening of skin color, weakness, malaise, tendency to hypoglycemia, polydipsia and polyuria, etc.

For the most part, differentiation between primary and secondary hypothyroidism is not exceedingly difficult. Certainly, history of prior radioactive iodine therapy, subtotal thyroidectomy or a goiter compatible with end-stage chronic lymphoid thyroiditis tends to exclude a pituitary etiology. A family history of thyroid disease, a very high serum cholesterol level and absence of history and physical findings compatible with either loss of other pituitary hormones or associated etiologies should, likewise, make one think of a primary thyroid cause. Symptomatically, patients with primary thyroid failure appear to be more severely affected. This probably results from a more complete thyroprivic state in the primary variety of hypothyroidism.

One can certainly undertake an exhaustive endocrine workup in patients suspected of pituitary hypofunction. This ranges from simple gonadotrophin determinations on a 24-hour urine specimen (FSH) to insulin induced hypoglycemia or arginine stimulation of growth hormone secretion to test for pituitary functional integrity. Further, a TSH stimulation test may be performed by giving the patient 5-10 units of intramuscular porcine TSH and measuring the 24-hour RaI uptake and serum T4D (or PBI) values before and after injection. Theoretically, because TSH acts by both increasing glandular uptake of iodine and release of thyroid hormones, these values should increase in secondary but remain unchanged in primary hypothyroidism. In actuality, however, a thyroid gland that has been endogenously understimulated due to pituitary insufficiency may require several days of TSH administration to produce significant changes in these parameters. For this reason, TSH stimulation is seldom used in our laboratory. In our experience, a simple, inexpensive and highly reliable *screening* procedure is the water-loading test. To perform this test of adrenocortical activity, the patient must be kept lying in bed during this procedure. He ingests 1500 c.c. of water shortly after arising and voiding in the A.M. All subsequent urine specimens are then collected and pooled over a five-hour period. Total urinary excretion over 800 c.c. tends to rule out pituitary disease. A word of caution is required. Hypopituitary patients may retain a large portion of this ingested water. For this reason, the patient should be monitored during the test by blood pressures to detect a state of water intoxication. If this occurs (which it rarely does), the therapy is intravenous hydrocortisone.

Fig. 11. Photograph of a patient with rheumatoid arthritis and typical features of myxedema due to chronic lymphoid thyroiditis (Hashimoto's struma).

Symptoms related to lack of thyroid hormones, as mentioned previously, are manifold and multisystemic (Figs. 11, 12). Skin tends to be thick, boggy and coarse, and features tend to be accentuated. There is a delicate periorbital puffiness. The tongue becomes thick and hair becomes brittle and coarse. Alopecia of the lateral margins of the eyebrows is not uncommon and nails become brittle and slow growing. There is generalized weakness and lethargy. Mentation and speech become slow and behavior can become erratic and at times irrational ("myxedema madness"). This may be aggravated by a dilutional hyponatremia secondary to inappropriate secretion of antidiuretic hormone (ADH). Weight gain (secondary to fluid accumulation) usually occurs in the presence of anorexia. Constipation is very common and gallbladder disease (possibly related to prolonged hypercholesterolemia) occurs more often than in normal subjects. This same association appears to predispose affected patients to coronary artery disease and generalized arteriosclerosis. Serous effusions, including pleural, pericardial and ascitic can occur. A large heart secondary to

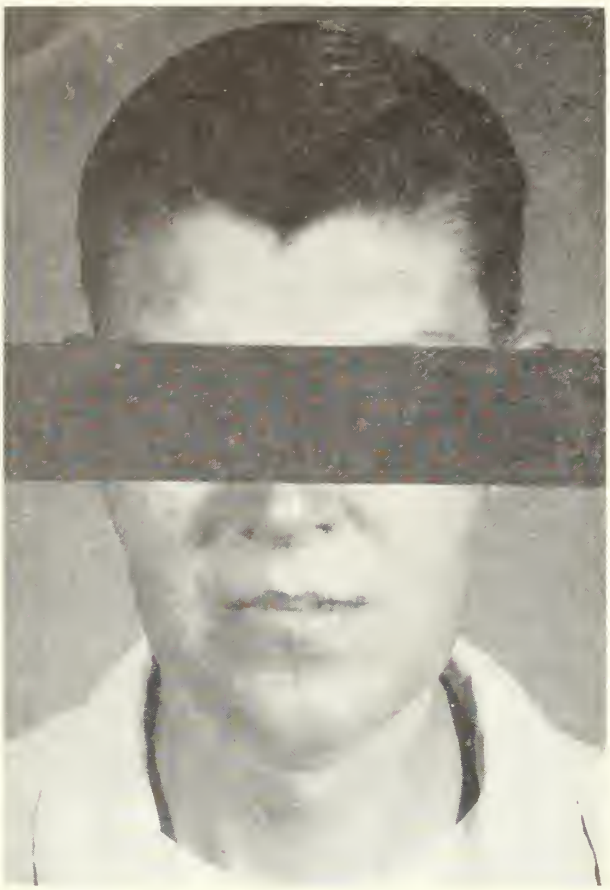

Fig. 12. Photograph of a patient with pituitary myxedema (panphypopituitarism) due to hemochromatosis.

pericardial effusion and a flaccid myocardium as well as other fundings suggestive of congestive heart failure have led to the term "myxedema heart." A "flat" oral glucose tolerance curve, decreased sensitivity to insulin, hyper and polymenorrhea, decreased libido, impotence and galactorrhea have been described. An anemia is invariably present in moderate to severe cases and is due to a variety of factors: a) diminished erythrocytic synthesis secondary to decreased tissue oxygen requirements; b) a nutritional anemia associated with anorexia and generalized inanition; c) B-12 deficiency secondary to pernicious anemia, which occurs more frequently in patients with primary hypothyroidism; and d) iron deficiency secondary to hypermenorrhea and polymenorrhea, often aggravated by insufficient oral replenishment of bodily iron stores.

The diagnosis of hypothyroidism is not difficult to make. In addition to the above mentioned history and clinical factors, the most useful laboratory tests are a T4D (or PBI provided there is no iodine contamination) and a resin uptake test (RT3 or RT4) from which the free thyroxine index (FTI) can be calculated. The free thyroxine index (FTI) is low in myxedema. In pregnancy or under estrogenic stimulation in patients with myxedema, the T4D may be in the normal, non-pregnant range but under these circumstances, the RT3 or RT4 is usually *extremely low* so that the FTI (the product of the T4D and resin uptake) will be low and diagnostic of hypothyroidism. Conversely, if the TBG in a hypothyroid patient is abnormally depressed (androgens, corticosteroids, chronic illness) or its binding sites occupied by drugs (salicylates, hydantoins) the RT3 or RT4 values may be normal or low normal, but the T4D values will be depressed even further (if possible) and the FTI will be in the hypothyroid range.

The 24-hour ^{131}I uptake (assuming the absence of factors which could give either a false positive or false negative value) is low in both primary and secondary hypothyroidism. But as previously mentioned, this test may be increased by administration of exogenous TSH in some cases of secondary hypothyroidism. In very rare instances, the RaI uptake may be normal or even elevated. These include "end stage" Hashimoto's thyroiditis where a "dying" gland is able to trap iodine but cannot efficiently make thyroxine. Another example of high RaI in the presence of hypothyroidism is the group of congenital metabolic thyroid diseases in which the gland can take up iodine, but the remainder of thyroxine synthesis of hormonal iodine is impeded due to genetic interferences with synthesis.

Ancillary parameters include a complete blood count (CBC) which could reveal the previously alluded to anemia, red blood cell indices, reticulocyte count and serum iron, B-12 and folic acid levels. These help to pinpoint any existing hematologic deficiency. If indicated, gastric acidity and a Schilling test can be performed. The electrolyte pattern could reveal a dilutional hyponatremia or a respiratory acidosis if the CNS is so compromised as to produce an hypoventillatory state. There is increased creatine and slightly increased tyrosine tolerance in hypothyroidism. Cholesterol is elevated in primary but may be normal in secondary hypothyroidism. Nonetheless, long-term anorexia or hepatic impairment can reduce the cholesterol level even in the primary variety. The BMR is low and the relaxation phase of the deep tendon reflexes is hypoactive in hypothyroidism.

Therapy of the hypothyroid state is one of the simplest, yet most rewarding aspects of medical therapeutics. When pituitary insufficiency has been excluded, all that is generally required is the simple oral administration of replacement doses of a natural or synthetic thyroid hormone preparation. This is one of the few instances of deficiency therapy when an inexpensive hormonal preparation given by mouth will produce full return to normalcy without any complicating side-effects or pharmacologic toxicity. Unfortunately, there is needless confusion pertaining to which specific thyroid preparation to use and how to interpret the resulting serum tests of thyroid function. The intact thyroid gland normally synthesizes a mixture of L-thyroxine and L-triiodothyronine in about a 3:1 ratio. It thus seems reasonable to assume that adequate hormonal replacement in a com-

parable ratio would result in clinical euthyroidism and normal values of serum T4D (PBI) RT3 or RT4 and hence, of FTI (Tables 2 and 3). Sodium L-triiodothyronine (Cytomel) on a per weight basis is about 3-4 times more potent calorigenically than T4; thus, placing a patient on small amounts (75-125 mcgm/day) of this hormone alone would render him euthyroid. But, under these circumstances, the serum T4D (PBI) values would remain in the low hypothyroid range. On the other hand, the resin uptake tests (RT3 or RT4) would be normal. Sodium L-thyroxine (Synthroid®, Letter®), conversely, elevates the T4D (PBI) values as well as the resin uptake tests into the hyperthyroid ranges while maintaining the eumetabolic state. Thus, when either synthetic T3 or T4 preparations are used *alone,* the free thyroxine index (FTI) is not a valid indicator of clinical thyroid function. For all this confusion, there is little advantage in using these synthetic preparations alone if one wishes to follow the therapeutic course with such patients by laboratory tests.

Desiccated thyroid, USP, have been a reliable thyroid hormone preparation for over half a century and until recently, was for most physicians the preparation of choice. If desiccated thyroid, USP, is prepared by a reliable firm that uses biological standardization along with chemical assay, adequate therapeutic amounts of this drug are sufficient in single daily dosage to maintain the euthyroid state in the presence of relatively normal serum parameters of thyroid function. Unfortunately, chemical standardization of desiccated thyroid is erratic and unreliable, so that there are presently on the market many preparations which meet the USP requirements but which have inadequate hormonal quality or calorigenic potency. To obviate biologically impure or erratic animal thyroid preparations, we have developed a synthetic combination in our laboratory (liotrix, Euthroid®-Warner-Chilcott) that contains sodium L-thyroxine and sodium L-triiodothyronine in a 4:1 ratio. Employment of this agent for thyroid hormone replacement is optimal in that it not only ensures the maintenance of the clinical euthyroidism but also gives meaningful serum parameters of thyroid function commensurate with the patient's metabolic state (Table 5).

Caution must be exercised in the initial treatment of the myxedema. The degree of caution depends on the extent and duration of insufficiency and the age and physical well-being of the patient. In general, we seldom initiate therapy with more than the equivalent of 30 mg. USP desiccated thyroid daily. This dosage can be increased by 30 mg. (or its equivalent in the synthetic liotrix mixture) daily every two to four weeks. The therapeutic objective for full replacement of thyroid hormones is usually between 90-180 mg. daily of USP thyroid or liotrix as tolerated. The most reliable indicator of euthyroidism in patients receiving the calorigenic equivalence of 90-180 mg. USP thyroid daily is the subjective response of the patient to a specific daily dosage. If this dosage is not tolerated because of angina or heart failure, the maximal therapeutic dosage that keeps the patient free from untoward symptoms is used.

TABLE 5

DOSAGE EQUIVALENCY OF COMMON THYROID HORMONE PREPARATIONS

Generic and Proprietary Designations	*Daily Dosage Range (mg)*	*Laboratory Parameters**		
		T4D	*RT3*	*FTI*
Desiccated Thyroid, USP (Armour Laboratories)	90-180	N	N	N
Levothyroxine Sodium (Synthroid, Letter)	0.25-0.40			
Liothyronine Sodium (Cytomel)	0.075-0.125		N	
Liotrix (Euthroid)	1½ - 3**	N	N	N

* N = normal; = increased; = decreased

** The numbers indicate the calorigenic equivalency (in grains) compared to desiccated thyroid, USP. Thus, Euthroid-3 would be equivalent metabolically to 3 gr. desiccated thyroid, USP.

THE GOITROUS STATE

For many years, there has existed in the minds of many physicians a rather paradoxical confusion regarding the clinical management of goiters, nodules and thyroid cancer. On the one hand, there are the rather striking statistics from major medical centers concerning the high incidence of thyroid cancer in patients undergoing thyroidectomy of goiters for suspected malignancy. Some estimates indicate that from 10-25 percent of single thyroid nodules are cancerous. On the other hand, physicians know from personal experience, from mortality figures and from the commoness of goiters and the rarity of thyroid cancers that these figures are misleading and inconsistent with their clinical observations. Despite many years of surgical therapy of goiters and nodules, there is little to show for any change in statistical benefits from surgical excision as opposed to either no therapy or thyroid suppression. Since this is a rather complex subject because of poor statistical data, the remainder of this presentation will deal with our views regarding management of goiters, nodules and thyroid cancer.

Goiter is a common disorder in this country with estimates as high as 5 to 10% of the population having thyroidal enlargement at some time in their lives. The incidence varies with geographic location, a higher number of goiters existing in certain "low iodine" regions around the Appalachian range, the Great Lakes region extending into the Pacific Northwest. Goiter, by definition, denotes an abnormal enlargement of the thyroid gland. It does not specify metabolic state. In fact, goiter may be associated with hyperthyroidism, hypothyroidism or euthyroidism. We have mentioned previously that hyperthyroidism is associated with both diffuse hyperplasia or multinodular goiter. Primary hypothyroidism is also associated with goiter, particularly in iodine deficient regions or in patients with chronic lymphoid thyroiditis (Hashimoto's struma). Large goiters are also

found in hypothyroidism secondary to inborn defects in thyroidal metabolism. By and large, goiters are most commonly seen in euthyroid individuals. Indeed, in such patients there are probably genetically related synthetic defects in portions of the thyroid having increased sensitivity to TSH such that diffuse or discrete zones undergo hyperplastic metamorphosis. This, coupled with a relative degree of iodine deficiency, could produce a full-blown goiter from a latent synthetic defect. In fact, the prime reason for the high occurrence of endemic goiter in certain relatively isolated geographic areas may be related to the perpetuation of such a genetic trait exaggerated by dietary factors. Regardless of the etiology, thyroidal enlargement to goitrous size is a compensatory phenomenon brought about by trophic efforts to stimulate thyroid hormone synthesis and secretion. If for any reason, the thyroid gland is unable to produce sufficient thyroid hormones to maintain circulatory and cellular supplies, pituitary thyrotropin (TSH) is activated in an effort to overcome this chemical defect (Fig. 1). By constant TSH stimulation, the thyroid hypertrophies until it reaches a new size capable of maintaining normal synthesis and secretion. Failing this, TSH secretion continues as a constant stimulus to goitrogenesis. In the absence of pituitary TSH, no goitrogenesis occurs. Pituitary TSH secretion can be inhibited selectively by full thyroid hormone replacement in doses equivalent to 120-180 mg. USP thyroid daily.

All individuals probably have some genetic propensity to develop goiter although the penetrance and degree of expressivity of this trait is probably greater in endemic areas. For some reason, there is a higher incidence of goiter in women and in older age groups. The theory established by Marine states that goitrogenesis is strongly associated with iodine deficiency. Constant waxing and waning in thyroidal iodine supply tends to promote growth and regression of hyperplastic areas, mediated by a TSH dependent pituitary-thyroid feedback loop. The longer one lives, the more likely is goitrogenesis to develop. Women are more predisposed at an earlier age in part, at least, because pregnancy and the menstrual cycle represent periods of fluctuating iodine economy.

Along with the endemic variety, sporadic and goiter secondary to Hashimoto's thyroiditis (chronic lymphoid thyroiditis) comprise the most common etiologies of nontoxic goiters. In addition, goiter can arise or be enhanced by ingestion of certain goitrogens which are present in such common foods as cabbage, turnips and kale; and in some medicinals, including PAS, resorcinol and some hypoglycemic agents (carbutamide). Concerning dietary goitrogens, they have to be ingested in significant quantities to be of clinical consequence. Concerning medicinal goitrogens, the mechanism of goitrogenesis is the same as in the treatment of the hyperthyroid state: inhibition of the organization step in the synthesis of thyroid hormones. Nonetheless, given to normal individuals, or in excessive dosage to hyperthyroid patients, the net production of thyroxine can be so diminished as to cause an increase in pituitary TSH, which, in turn causes hyperplasia of the thyroid gland. Administration of thyroid in replacement dosages in concert with antithyroid drugs will obviate goiters caused by the goitrogenic compounds.

Unless the goiter is sufficiently large to produce local symptomatology by mechanical compression (e.g., hoarseness, dysphagia, stridor), or unless it presents a significant cosmetic problem, the only treatment we recommend is exogenous thyroid hormones in full suppressive doses. Even then, we usually reserve treatment to those individuals whose thyroid glands are larger than twice normal size in whom the diagnosis is made before middle age. Of course, the patient's state of health must permit use of full suppressive doses of thyroid. Thyroid hormone therapy is given to goitrous patients for three distinct reasons: a) to prevent further goitrous growth by suppressing endogenous TSH; b) to induce anatomic regression of the goiter size; and c) to obviate possible hypothyroidism in certain goiters such as with Hashimoto's thyroiditis. Before initiating therapy, it is useful to obtain a T4D, resin uptake test, a 24-hour RaI and, where indicated, a thyroid scan. If there are discrete "hot" nodules seen on scan, and particularly if serum thyroid parameters are high normal, a thyroid suppression test is helpful in the early diagnosis of Plummer's disease (toxic nodular goiter). If there is no significant thyroid suppression, these patients should be watched carefully or treated for mild thyrotoxicosis as indicated.

To capitulate, small diffuse goiters should be treated with full suppressive doses of thyroid as should multinodular goiters which are nontoxic. Surgical therapy for nontoxic goiters should be limited to those rare occasions when clinically significant, documentable trachael or esophageal impairment can be demonstrated. Once excision of nontoxic goiter has been completed, patients should be maintained on full doses of thyroid hormones to prevent regeneration of residual remnants. Surgery does not alter the abnormal glandular tissue remaining. Unless protected against further stimulation from TSH, these goitrous remnants will recur with time, or if not, may atrophy to produce postoperative hypothyroidism. This latter occurrence is especially true after thyroidectomy for goiters due to chronic lymphoid thyroiditis (Hashimoto's struma).

Thyroid nodules, and particularly single thyroid nodules, require special emphasis in a general discussion of goiter. This distinction is particularly appropriate because of the special diagnostic steps required for individualizing therapy. Thyroid nodules are often neoplasms, and under these circumstances the question of thyroid cancer becomes a prime consideration. Because of the emotional response generated, even in some physicians' minds, to the term *cancer,* this subject has received greater emphasis than deserved by its rightful place in the morbidity and mortality list of human cancers. A few general statistical facts should be appreciated in order to place thyroid cancer in proper perspective.

TABLE 6

GUIDELINES FOR A RATIONAL APPROACH TO MANAGEMENT OF THYROID NODULES

Fact	*Guideline*
1. Single nodules are more likely to harbor occult neoplasms than multiple nodules.	1. Single nodules in appropriately selected patients should be removed.
2. "Cold" nodules are more likely to harbor occult neoplasms than "hot" nodules.	2. "Cold" nodules in appropriately selected patients should be removed.
3. The incidence of nodular goiter is ten times greater in females while the incidence of thyroid cancer is only four times greater than in males.	3. All male patients with single nodules should be considered for surgery.
4. Despite physical and radioisotopic evidence of a single thyroid nodule, the thyroid gland can harbor multiple nodules. This is more likely to be present in the older age group.	4. Younger individuals with single nodules should be considered for surgery. Older individuals with "single" nodules often have multinodular goiter.
5. Nodules which regress on thyroid hormone suppression are probably not malignant.	5. If criteria for immediate surgery are not met, a trial of thyroid hormone suppression is indicated.
6. Thyroid hormone suppression, by diminishing TSH release, probably suppresses nodular growth.	6. All patients not meeting surgical criteria should be placed on exogenous thyroid hormone in adequate suppressive doses, when tolerated.

First, while the incidence of nodular goiter is extremely common (over 40,000 per million population in the United States), the incidence of thyroid carcinoma is rare (25 per million). Second, the diagnosis of thyroid cancer can only be made with certainty by *excisional* biopsy. This is unlike other neoplasms where such ancillary aids as exfoliative cytology and roentgenologic methods are available. Excisional biopsy for all intents represents a "cure" in the majority of cancers. At the very least, the natural history of this disease is irreversibly altered by excision. Third, patients who undergo thyroid surgery for cancer are a highly selected group; that is, they are selected for surgical excision on the basis of some sign or symptom suggesting at least a suspicion of thyroid cancer. This produces a high incidence of cancer per surgical operation for cancer because of biased selection. Fourth, while there are four general histopathologic patterns of thyroid carcinoma (papillary, follicular, medullary with amyloid struma and anaplastic), from a clinical point of view, the first two represent the commonest clinically encountered varieties and, fortunately, are relatively benign. The latter two are rare and, unfortunately (especially the last), are quite devastating. Thus, many physicians accept the observation that no matter what surgical procedure is performed, the clinical course of all four, and especially the papillary and undifferentiated varieties, remains unaltered. In other words, patients with papillary carcinoma (the most common thyroid malignancy) will probably not succumb to their disease while patients with anaplastic carcinoma (the least common thyroid malignancy) eventually will succumb regardless of therapy. The reader should not conclude that this represents a nihilistic therapeutic philosophy. It is merely recognizing that the art of medicine places the physician in a difficult position and he must often sail between the mythological Scylla and Charybdis. Nonetheless, there are certain guidelines that enable one to screen patients suspected of harboring a thyroid malignancy in order to make at least a rational approach to therapy. Some facts and guidelines to therapy of thyroid nodules are presented in an oversimplified form in Table 6.

While certainly not an ultimate or fool-proof approach to management of the nodular thyroid, we feel that this approach represents a positive "middle-of-the-road" position. It differs on the one hand, from the extreme of needless surgical extirpation of all thyroid nodules and on the other, the *laissez-faire* attitude of therapeutic abstinence. In our experience, this policy has, to date, yielded the highest number of salvageable thyroid cancers for the lowest number of surgical procedures.

QUESTIONS AND ANSWERS

Q. Have situations been described where the thyroid gland preferentially produces only T3?

A. Yes, there are two situations, both rare, in which this occurs. In one, there is severe iodine deficiency such as when the efficiency of the gland has been compromised, as in the immediate postradioactive iodine therapy period. Looking at it teleologically, the synthesis of T3 requires one less iodine atom per molecule than T4. In the presence of inadequate amounts of iodine, or when a destructive process reduces thyroxine-making efficiency, there appears to be a predisposition to bring out this reserve potential in the thyroid; namely, the ability to function at a lower level of activity by producing a smaller amount of a more potent hormone, namely T3.

Why the thyroid does not normally use this "easier way out" is not clear. There are intra-thyroidal autoregulatory mechanisms to prevent the gland from oversynthesizing in the presence of iodide excess, thus preventing thyrotoxicosis. In an analogous manner, there appear to be mechanisms for preserving iodine and still providing adequate hormones by preferential synthesis of T3 under special circumstances. Indeed, the second situation in which preferential production of T3 does occur excessively and autonomously is the rare T3-toxicosis. We have recently described this phenomena in conjunction with Dr. Kenneth Sterling of Columbia

University who has developed a technique for the accurate measurement of circulating T3 levels. Unfortunately, this diagnosis cannot be made using the standard FTI calculation. In this rare disease state, serum T4D and PBI values are normal and RT3 and RT4 values are usually in the normal or high range. The RaI, however, is usually elevated or the upper limits of normal; but more important, the gland is non-suppressible. These factors, coupled with the patient's history, the presence of thyroid nodules on physical examination and "hot" nodules on scan should make one suspicious of this entity.

Q. You appear to be downgrading the value of the PBI. Should this test ever be performed if one has access to the serum T4D?

A. Very rarely. One unique situation that comes to mind is the case of the individual suspected of hyperthyroidism who has borderline elevated T4D and RT4 values and whose RaI is not as elevated as would be expected. The finding of a significant discrepancy between T4D and PBI (or total iodide) would indicate that the falsely depressed RaI was due to the presence of exogenous iodide and would lead one to more strongly suspect hyperthyroidism. Of course, lack of discrepancy between T4D and PBI in an individual with a low uptake could also be caused by thyrotoxicosis factitia.

Q. If, for reasons alluded to, the pregnant hyperthyroid patient cannot or does not take her antithyroid medication, what else can be done?

A. There are not too many options available under these circumstances since there are only three methods of treating hyperthyroidism. Radioactive iodine is contraindicated in pregnancy because of the potential radiation hazzard to the fetus. This leaves surgery as the only other option. This is best performed in the latter part of the second trimester. The patient can be prepared preoperatively with PTU or Tapazole® (if possible) and iodine supplements given according to the manner described previously. Fetal goiter, even leading to strangulation, has been reported in pregnant mothers given large amounts of goitrogens or iodides, but this does not occur if the mother is never allowed to become hypothyroid and the course of pre-operative treatment with iodide is relatively short (less than two weeks).

Q. Not uncommonly, one sees patients who are placed on small (¼ or ½ grain) or very large (5 or 6 grain) doses of thyroid. Would you comment on this?

A. Unless you are titrating a hypothyroid patient and are gradually increasing the dosage, there is no physiologic rationale for giving less than full hormonal replacement. That is the equivalent of 2 to 3 grains of desiccated thyroid daily. If you give ¼ grain to a euthyroid individual with an intact pituitary-thyroid axis, all you are accomplishing is reducing his normal endogenous production of thyroid by ¼ grains of thyroid per day. As the pituitary responds to circulating free thyroxine levels, this small amount of exogenous hormone will slightly suppress TSH production, but the *net* amount of bodily thyroxine will be the same. Hence, when giving small doses of thyroid, you are neither increasing endogenous hormonal levels, if you desire this, nor are you "resting" the gland, if this be your motive.

Greater than physiologic amounts, on the other hand, are of no useful therapeutic value. If you are giving pharmacologic doses of thyroid for weight reduction, you will end up with a fat but nervous patient! Further, it is surprising how much thyroid hormone is necessary to produce thyrotoxicosis factitia. Many patients with Graves' disease are producing the equivalent of thirty grains of desiccated thyroid daily.

Q. Would you briefly describe the management of hypothyroidism and coronary insufficiency?

A. There are many facets to this question. As you know, radioactive iodine was used in the past for the treatment of uncontrollable angina and congestive heart failure. The rationale for this was to diminished cardiac consumption and decreased peripheral metabolic demands for oxygen on the assumption that this would reduce the cardiac burden. Indeed, this treatment was effective in selected patients, but at a very great price. The patient was buying symptom-free time at the price of increased sluggishness, mental dullness, lethargy and perhaps a hastening of the atherosclerotic processes that originally contributed to his symptomatology. Fortunately there are now drugs (B-adrenergic blockaders, coronary vasodilators, diuretic agents), mechanical devices (electrostimulators of the carotid sinus) and surgical techniques (vascularization procedures, valve replacements) that render such thyroid ablative therapy archaic.

On the other hand, hormonal replacement of the hypothyroid patient with concomitant ASHD is a serious and real problem. It is not uncommon because myxedema occurs in older individuals and because the myxedematous state, with concomitant hypercholesterolemia, is associated with aggravation of the arteriosclerotic process. One must titrate the tolerance of the patient to the thyroid dosage by observation of clinical symptoms. Here, again, the physician is sailing between Scylla and Charybdis. The use of Cytomel in such instances is useful; but because of the rapid surge of action of this fast-acting hormone, we prefer desiccated thyroid or Euthroid (liotrix-Warner-Chilcott). Initial dosage of thyroid under these circumstances is 1/8 to ¼ grain daily by mouth, increasing, as tolerated by 1/8 to ¼ grain increments daily every 2 to 4 weeks.

Q. You just mentioned the use of B-adrenergic blocking agents and I have recently read of their use in the management of thyrotoxicosis. Would you comment?

A. The role of adrenergic blocking agents, as an ancillary measure in the management of the thyrotoxic individual has recently been tried to control cardiac symptoms, particularly palpitations. As the thyrotoxic state is one of increased sensitivity to catecholamines, the use of these agents is of value in diminishing myocardial activity. In fact, we are in the process of evaluating a new

B-Adrenergic blocking agent (Sotalol) that appears to have only negative chronotropic and no negative inotropic effects on the heart. One word of emphasis: these agents provide only transient symptomatic relief. The only definitive cure for thyrotoxicosis is to treat the thyroid gland, not the symptoms.

Q. How do you manage the severely thyrotoxic patient or the patient with myxedema coma who has a concomitant acute surgical problem?

A. You are referring to two of the most catastrophic situations in medical therapeutics. Let us examine thyrotoxicosis first. A surgical emergency in a patient with uncontrolled thyrotoxicosis is a serious emergency since it usually precipitates a "thyroid storm." Under these circumstances, mortality is high no matter how carefully therapy is selected. The physician is faced with a surgical condition in a patient not suited to operative intervention. If the operation can be postponed to permit time to control the thyrotoxicosis, this will permit a better salvage rate. We treat thyroid storm with four aspects in mind: a) to diminish synthesis of thyroid hormones as rapidly as possible; b) to diminish release of thyroid hormones from the gland; c) to diminish the clinical manifestations of circulating thyroid hormones; and d) to provide ancillary medical care. For the first two aspects, we prescribe large doses of antithyroid drugs (e.g. 200-300 mgm of PTU q 6h) and iodine (NaI solution 500 mg intravenously in 100 cc. of 5% G/W). The third measure includes sedation, ice mattress, catecholamine depleting if indicated (e.g. reserpine, guanethidine) and blocking agents (e.g., propranalol). The fourth, corticosteroids (400 mgm hydrocortisone during the first 24 hours and diminishing by 100 mgm q 24 hours), multi-vitamins and adequate nutrition (glucose). Shock, if present, should be treated accordingly. Unfortunately, we cannot improve on this regime even if the patient does have an acute abdomen. There is obviously a significantly high mortality in thyroid "storm," but if the patient requires surgery, it should be performed as quickly and efficiently as possible under minimal anesthesia.

Myxedema coma is devastating enough (all three of our last so afflicted patients succumbed) without any surgical complication. We generally treat the patient as we would uncomplicated myxedam coma with thyroxine 100 mcgm intravenously q 6 h for 4-6 doses and gradually decrease this to 50 mcgm by mouth as tolerated by the patient. If hypoventillation and its complications are present, these are treated accordingly. Unless evidence is overwhelming to the contrary, the patient with myxedema coma is assumed to have pituitary insufficiency as the etiology. Hydrocortisone is given to the myxedematous patient in coma in appropriate dosage. The diagnosis of pituitary insufficiency can always be ruled in or out at a later time. Preoperative medication and anesthetic agents should be administered in less than normal doses to hypothyroid patients because of their prolonged half-life under these circumstances.

Q. Does the addition of thyroid hormones to the therapeutic regime help the exophthalmos in a patient with Graves' disease?

A. We don't know what helps exophthalmos in Graves' disease but some conditions, such as hypothyroidism make it symptomatically worse. There is no direct correlation between degree of thyroidal and nonthyroidal manifestations and LATS. We cannot predict which patients will develop significant ophthalmopathy and which will not. In answer to your question, addition of thyroid hormone does not appear to alter the course of exophthalmos, but we feel it is important to give since it prevents hypothyroidism and the treated hyperthyroid patient is thus maintained in a better state of euthyroid balance.

Acknowledgement

The authors acknowledge with gratitude the contributions to the studies reported in this review of Drs. Samuel Refetoff and Victor Fang and to Mr. Robert Hagen. Their creative contributions to measurements of thyroid hormones in serum have improved the diagnostic resources of all physicians.

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DEAN H. FISHER, M.D.
COMMISSIONER

State Of Maine

Department of Health and Welfare

Diagnosis and Treatment of Organophosphate Insecticide Poisoning

G. B. EPSTEIN*

Highly toxic organophosphate insecticides such as Parathion, Malathion and Guthion are being used increasingly in the agricultural community because such pesticides break down more rapidly than the environmentally persistent chlorinated hydrocarbons such as DDT, Endrin, and Dieldrin. This is of interest to the medical profession, both because of the rapid onset of symptoms of organophosphate poisoning and because a specific treatment exists for such poisoning, while treatment of chlorinated hydrocarbon poisoning is essentially symptomatic.

Organophosphates act primarily as cholinesterase inhibitors. According to Davis *et al*[1]: "The clinical manifestations of organophosphate pesticide poisoning are well described and include miosis, weakness and collapse, muscular fasciculations, cutis anserina, diaphoresis, pulmonary edema, nausea, vomiting and diarrhea. Unfortunately, not every patient evidences a set pattern of clinical response when first seen by a physician. The clinical signs may be confused with encephalitis, brain injury, hypertensive encephalopathy, pneumonitis, gastroenteritis, asthma and congestive heart failure, to name a few."

Cholinesterase inhibition may be determined by the method of Michel or by the pH stat method. Unfortunately, by the time samples are sent to a laboratory and processed, it is usually too late. Two inexpensive, rapid screening tests are available: the Acholest from Fougera and Co., Inc., Cantiague Road, P. O. Box 730, Hicksville, Long Island, New York, 11802 and the ChE-tel from Charles Pfizer and Co., Inc., 300 West 43rd Street, New York, New York, 10036, which may be used as diagnostic aids.

Treatment, as recommended by Hayes,[2] is as follows: I. In very severe cases, the order of treatment should be as follows: (1) *Artificial respiration,* if required, preferably by mechanical means. (2) *Atropine Sulfate,* 2 to 4 mg. (1/30 to 1/15 grain) intravenously as soon as cyanosis is overcome. Repeat at 5 to 10 minute intervals until signs of atropinization appear, (dry, flushed skin and tachycardia as high as 140 per minute). (3) 2-PAM,[3] SLOWLY intravenously, 1 g. for adults and 0.25 g. for infants. (4) *Decontamination* of the skin, stomach and eyes as indicated. (5) Symptomatic treatment.

II. In the more usual cases, proceed as follows: (1) *Atropine Sulfate,* 1 to 2 mg. (1/60 to 1/30 grain), if symptoms appear. If excessive secretions occur, keep the patient fully atropinized. Give atropine sulfate every hour up to 25 to 50 mg. in a day. (2) *Decontamination* of the skin, stomach and eyes as indicated. (3) 2-PAM, SLOWLY intravenously, if the patient fails to respond satisfactorily to atropine sulfate. Dose of 1 g. for adults and 0.25 for infants. (4) Symptomatic treatment.

The Public Health Laboratory, of the Department of Health and Welfare, is fully equipped for the determination of pesticides, both in tissue samples and in fluids from gastric lavage, urine and blood, for confirmation of pesticide poisoning.

The two publications listed under References are highly recommended. It is also recommended that one of the screening tests for cholinesterase inhibition be obtained for hospital diagnostic labs and that a supply of the drug 2-PAM be on hand. A film entitled "Diagnosis and Treatment of Organophosphate Insecticide Poisoning" is also available for medical personnel from the Film Library of the Department of Health and Welfare.

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3. 2-PAM is available from Ayerst Laboratories, 685 Third Avenue, New York, New York 10017.

AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

Businessmen Launch Drive Urging Regular Physical Checkups

ATLANTA, GA. — A businessmen's organization is launching a nationwide drive urging its members to get regular physical checkups including cancer tests.

The project was jointly announced here recently by the National Exchange Club and the American Cancer Society during the Club's annual convention. The meeting of educational service executives was addressed by Dr. A. Hamblin Letton, Chairman of the Society's Medical and Scientific Committee, and Attending Surgeon and Chief of Staff, Georgia Baptist Hospital, Atlanta.

The educational campaign in cooperation with the Society will urge NEC's more than 47,000 members to develop a lifetime habit of physical checkups with a "procto" test for intestinal cancer for those over 40.

In a letter to its presidents, the Club leadership said the project "grew out of our concern with the increasing death rate of men from cancer.

"The startling fact is that although cancer kills 55 American men to every 45 women, only 13 percent of men get regular checkups (including cancer tests) compared to 40 percent of the women. That is the challenge with which we are presented. It is to this program aimed at helping to save the lives of those who may die needlessly of cancer, that we have pledged our active support."

Affiliated clubs are being asked to keep a tally of members who have had checkups. Upon completion of the project, Clubs reporting from 75 percent to 100 percent of their members as having had checkups (including the procto) will receive specially designed certificates.

American Cancer Society News Service Release.

Necrologies

Marcel D. Ouellette, M.D.

1922-1970

Marcel D. Ouellette, M.D., 48, of Sanford, Maine died on July 10, 1970. He was born in Lewiston, Maine on February 26, 1922, son of Napoleon and Regina Ouellette.

Dr. Ouellette was graduated from St. Charles University in Sherbrooke, Quebec in 1944 and received his medical degree from Laval University Faculty of Medicine in 1950. He interned at the Quebec City Hospital from 1949 to 1950 and served a residency at McKeesport General Hospital in Pennsylvania from 1950 to 1951. Dr. Ouellette served as a Flight Surgeon in the U.S. Air Force during the Korean War from 1951 to 1953. In 1953, he located in Sanford and practiced there the past eighteen years.

He was a member and past president of the York County Medical Society, a member of the Maine Medical Association, and was a past president of the Henrietta D. Goodall Hospital staff and the Sanford Rotary Club.

Surviving are his widow, the former Esther LeClerc; two sons, Andre and Jean Jacques Ouellette; four daughters, Misses Joscelyne, Louise, Michelle and Renee Ouellette, all of Sanford; three brothers. Raymond, Roger and Omer Ouellette, all of Lewiston; and a sister, Mrs. Ralph Turgeon of Westbrook.

Harry M. Wilson, M.D.

1905-1970

Harry M. Wilson, M.D., 65, of Bath, Maine died on July 23, 1970. He was born in Berlin, New Hampshire on June 8, 1905, son of Alexander and Mary Ellen Wilson.

Dr. Wilson was graduated from Berlin High School, the University of Vermont, and received his medical degree from the University of Vermont College of Medicine in 1932.

Following his internship in Burlington, Dr. Wilson practiced medicine in Bethel from 1932 to 1942 and then served in World War II as Major for three years. He then located in Bath and in 1953 was recalled to active duty serving in the Korean War as Lieutenant Colonel. In 1954, Dr. Wilson returned to Bath, but remained in the Army Reserves and was promoted to full Colonel in 1960. During his military service, he received many awards including five battle campaign stars and a bronze star with citation for service in World War II. He received two battle campaign stars and an Oak Leaf Cluster to add to his bronze star for service in the Korean War. Dr. Wilson also received several citations and commendations from President Sigmond Rhee and the Generals of the ROK Army.

He was a member and past president of the Lincoln-Sagadahoc County Medical Society, a member of the Maine Medical Association and the American Medical Association. Dr. Wilson was also a member of the Founders Group of the American Board of Abdominal Surgery and a Fellow in the American Society of Abdominal Surgery.

Surviving are his widow, Mrs. Alberta White Wilson; one son, Harry, Jr. of Gardiner; one daughter, Mrs. Barbara Beck of Bucksport; one brother, George of Berlin, New Hampshire; and one sister, Mrs. Helen Rayner, also of Berlin; and five grandchildren.

Peter F. Lansing, M.D.

1924-1970

Peter F. Lansing, M.D., 45, of Augusta, Maine died on August 5, 1970. He was born in Berlin, Germany on August 19, 1924, son of Dr. George and Johanna Loewenstein.

Dr. Lansing was graduated from the University of Illinois and received his medical degree from the University of Illinois College of Medicine in 1947. He interned at the U.S. Marine Hospital in New Orleans from 1947 to 1948. Following two years at the Veterans Administration Center in Togus, he served a residency at the Newington Veterans Administration Hospital in Connecticut from 1951 to 1952 and the Veterans Administration Hospital in Albany, New York from 1952 to 1954. In 1954, Dr. Lansing located at the Veterans Administration Center in Togus where he served as chief of the pulmonary section.

He was a member of the Kennebec County Medical Association, the Maine Medical Association, the American Medical Association and was a fellow of the American College of Physicians.

Dr. Lansing is survived by his widow, the former Carolyn Louise Osgood of Augusta; his parents of Clearwater, Florida; a daughter, Miss Joan Carolyn Lansing of Augusta; a sister, Mrs. Roger Gallagher of Amherst, Massachusetts; one niece and one nephew.

Marcus A. Torrey, M.D.

1902-1970

Marcus A. Torrey, M.D., 67, of Ellsworth, Maine died on September 1, 1970. He was born in Steuben, Maine on December 9, 1902, son of Ernest and Bertha E. Torrey.

Dr. Torrey was graduated from Bates College in 1927 and received his medical degree from the Long Island College of Medicine in 1933. He interned at the Brooklyn Eye and Ear Hospital from 1933 to 1934. In 1935, Dr. Torrey located in Ellsworth where he practiced in otolaryngology.

He was a member of the Hancock County Medical Society, the Maine Medical Association and the American Medical Association. Dr. Torrey was also a consultant at the Castine Community Hospital and was on the staff of the Mount Desert Island Hospital in Bar Harbor and the Blue Hill Memorial Hospital. During World War II, he served as a Major in the Air Corps.

Survivors are his widow, the former Lona M. Greenleaf of Ellsworth, and his mother also of Ellsworth.

CALORIES / 7 oz. Serving*

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Consommé	29	Tomato	69
Chicken with Rice	43	Cream of Asparagus	70
Chicken Gumbo	48	Cream of Chicken	76
Chicken Noodle	54	Cream of Mushroom	115
Cream of Potato	58	Green Pea	116
Chicken Vegetable	60	Cream of Shrimp (Frozen)	132
Vegetable Beef	66	Bean with Bacon	133

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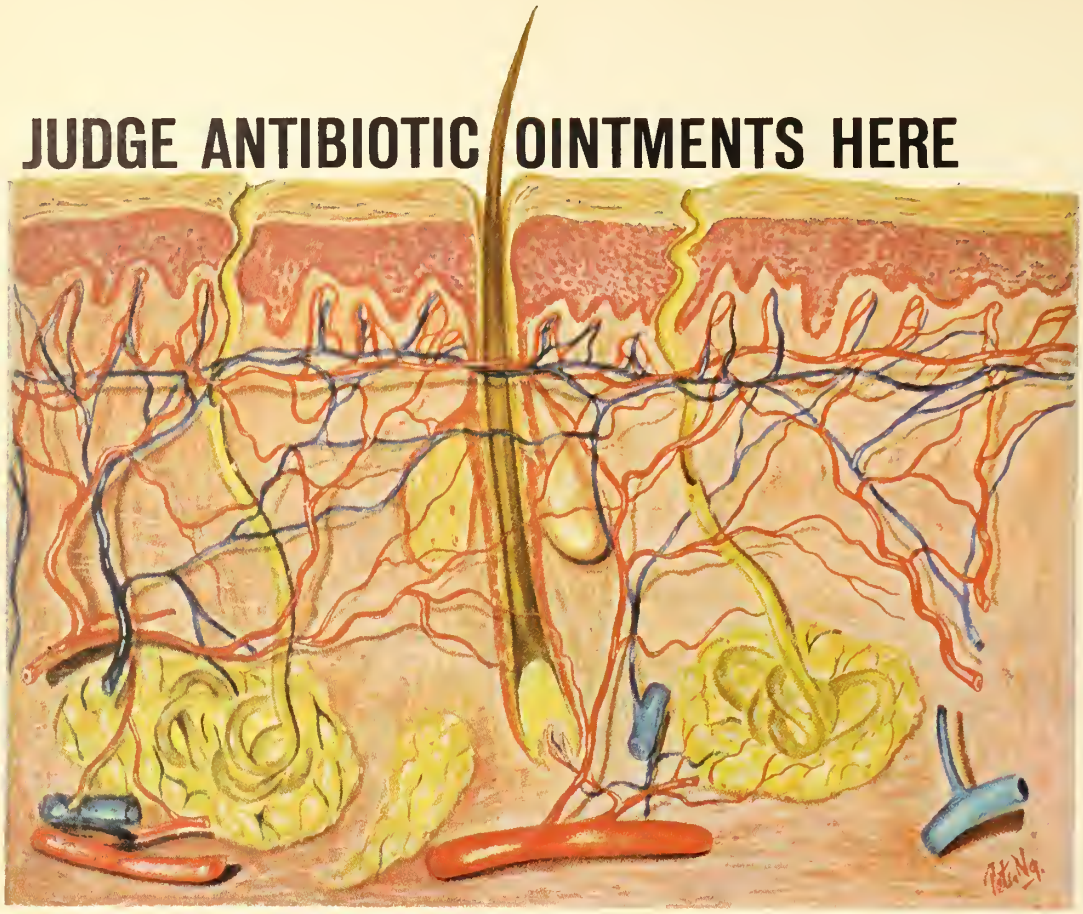

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Reduces swelling
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Indications: When used as adjunctive therapy for the rapid resolution of inflammation and edema, good results have been obtained in:
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Contraindications: ORENZYME BITABS should not be given to patients with a known sensitivity to trypsin or chymotrypsin.
Precautions: It should be used with caution in patients with abnormality of the blood clotting mechanism such as hemophilia, or with severe hepatic or renal disease. Safe use in pregnancy has not been established.
Adverse Reactions: Adverse reactions with ORENZYME have been reported infrequently. Reports include allergic manifestations (rash, urticaria, itching), gastrointestinal upset and increased speed of dissolution of animal-origin surgical sutures. There have been isolated reports of anaphylactic shock, albuminuria and hematuria. Increased tendency to bleed has also been reported but, in controlled studies, it has been seen with equal incidence in placebo-treated groups. (See Precautions.) It is recommended that if side effects occur medication be discontinued.
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TRADEMARK BITABS U.S. PATENT NO. 3,004,893 9/70 0-009A 161

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Letters to the Editor

To the Editor:

My work as a member of the Public Health Subcommittee in the U. S. House of Representatives has made me increasingly aware of a vital fact:

The health care needs of our nation can be met only by maintaining – and indeed expanding – the numbers of professional medical personnel available.

I am dismayed by the financial crisis confronting many of our medical schools, for only by assuring a continuing number of skilled graduates can we ever hope to have programs such as Medicare, Medicaid, and national health insurance provide our citizens with the health care which they now expect to receive.

I am especially concerned by the possibility that our government programs, and the trends towards "specialization" in our society as a whole, are overlooking the important role of the family physician in medical practice. To overcome this trend, I have introduced legislation which provides special incentives for the training of future family physicians.

At a time when too many of our relationships with others have become impersonal, I feel we must do everything possible to protect the confidence which should exist between patients and physicians. The family physician is one of the most important individuals to millions of Americans, and I believe his position must be strengthened. *All* professional physicians, however, need protection from unwarranted government intrusion in their practices.

For this reason, I have fought against many provisions in the proposed drug abuse control legislation before my Subcommittee. Whatever the need for strong enforcement legislation, I believe it more important that legitimate medical personnel not be hindered in their work.

For this reason, I have sponsored the national health insurance plan which best represents the role which professional medical personnel will play in this program.

For this reason, I pledge to continue to do everything possible in the Congress to assist our doctors, nurses, medical technicians, and administrators in bringing the best possible health care to our American citizens.

PETER N. KYROS
U. S. Congressman
First District, Maine

To the Editor:

Having worked with you and the Maine Medical Association in years past in the field of public relations and public information, I appreciate this opportunity to directly communicate with those in the State of Maine most directly and daily concerned with the condition of medical care for our citizens. The problems that are currently facing this country in the medical field are so immense, and the possible and even already suggested solutions so numerous and complex, that it is very difficult to discuss briefly in a letter what should properly be expounded upon at great length in an article or series of articles, but I do wish to state at least my basic feelings and approach as to what are the needs in this area.

I do not need to tell those of you who are working exhaustingly long hours every day that the problem of an adequate number of doctors is particularly acute in the rural areas, or that the problem of adequate medical care is particularly acute among the poor and aged, those who are most in need of medical care but are least able to meet the skyrocketing medical costs. It is a national problem, and it is well recognized by the current administration that the level of medical care in this country must not be allowed to continue to drift as it has for the past thirty years.

The Administration has already indicated that the status of health care will be a major concern and a topic of high priority in the forthcoming Congress; if elected, it will certainly be one of mine. There will be many proposals suggested and a lengthy debate involved. I do not pretend to know at the present time what the final solution must be, but will await a full discussion of all the suggestions, those of the Administration, as well as those of others, before making a determination.

I am opposed to the kind of universal socialized medicine that has already been proven not to work well in Britain, but I do believe that the Federal Government has a responsibility to insure that adequate health care is made available to all our citizens. I have already in this campaign called for a slowdown of massive Federal programs such as the space program, that need not be pushed with great urgency, so that some of these funds may be redirected toward the tremendously urgent human needs we are faced with at the present time.

The Nixon Administration itself has stated that spending in the health field will be almost twenty-eight percent higher in 1971 than in 1969. One area of highest priority to me, and to which I believe a substantial amount of funds should be diverted, is bio-medical research into the causes of heart disease and cancer. Major increases in funds to curb pollution and to alleviate drug and alcoholism problems should be made. And a desperate need for an increase in the supply of health resources – manpower and facilities – should be met.

In closing, I would like to assure you and the members of the medical profession in Maine that if elected in November, I shall do my best to work toward fair and adequate solutions to the health problems of the nation, and will consider such a commitment as of the highest priority.

RONALD T. SPEERS
Candidate, U. S. Congress
First District, Maine

American Medical Association to Sponsor 12th National Conference on the Medical Aspects of Sports

The 12th National Conference on the Medical Aspects of Sports, sponsored by the American Medical Association under the auspices of its Committee on the Medical Aspects of Sports, will be held in Boston, Massachusetts, at the Sheraton-Boston Hotel on November 29, 1970. The Conference is held annually in conjunction with and on the first day of the Clinical Convention of the American Medical Association.

As was true of the previous eleven Conferences, the 12th will cover a wide range of subjects of interest to those serving school and college athletic programs. Included will be forums and discussion sections relating to research in sports, aquatic sports, football rules and injuries, psychology in sports, girls in sports, and emergency and public health aspects of sports. At the Conference Luncheon, Francis D. Moore, M.D., Moseley Professor of Surgery, Harvard Medical School; Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston; and eminent deep-water skipper will discuss the topic "SAILING INTO TROUBLE." At the evening session, demonstrations on preventive and therapeutic taping, and musculo-skeletal aspects of pre-participation examination will be staged.

The Conference is open to key non-medical athletic personnel as well as interested physicians. Those who would like to receive further information concerning the Conference should address the Committee on the Medical Aspects of Sports, American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.

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24th AMA Clinical Convention in Boston, Massachusetts November 29-December 2, 1970

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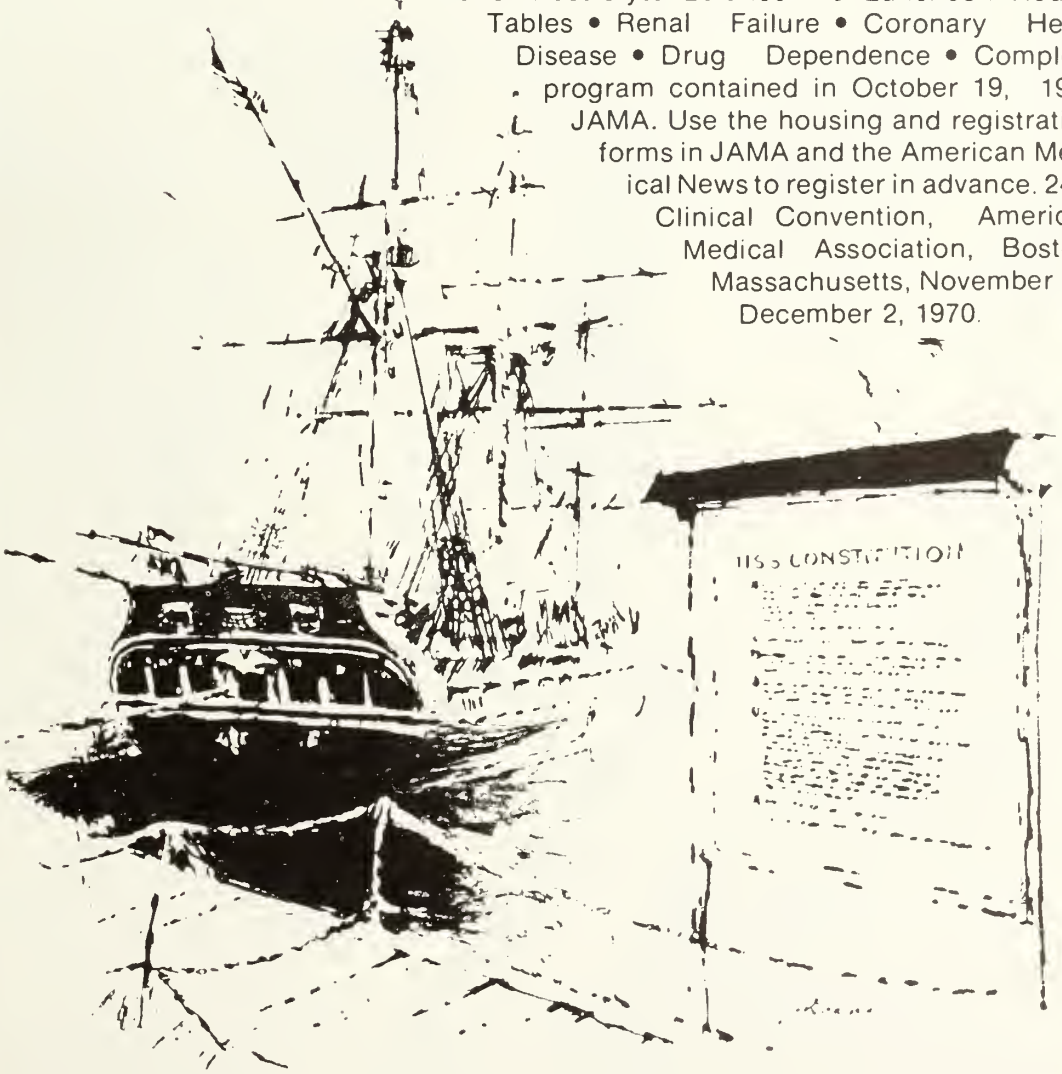

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*Slanger, A.: Med. Times *94*:150 (Feb.) 1966.

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spares the potassium

Before prescribing, see complete prescribing information in SK&F literature or *PDR*.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome, late pregnancy; also steroid-induced and idiopathic edema, and edema resistant to other diuretic therapy. 'Dyazide' is also indicated in the treatment of mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., certain elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—they can both cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules.

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BREAKUP—symbol of the impact of emotional stress. But when the stress exceeds transient rage or depression—and settles into a chronic mixed anxiety depression state—combined tranquilizer-antidepressant therapy could be indicated.

FOR MODERATE TO SEVERE ANXIETY WITH COEXISTING DEPRESSION

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TRANQUILIZER-ANTIDEPRESSANT

Containing perphenazine and amitriptyline HCl

For prescribing information, including indications, contraindications, warnings, precautions, and side effects, please see following page.

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TRIAVIL®4-25: Each tablet contains 4 mg. of perphenazine and 25 mg. of amitriptyline hydrochloride.

INDICATIONS: Patients with moderate to severe anxiety and/or agitation and depressed mood; patients with depression in whom anxiety and/or agitation are severe; patients with depression and anxiety in association with chronic physical disease; schizophrenics with associated depressive symptoms.

CONTRAINDICATIONS: Central nervous system depression from drugs (barbiturates, alcohol, narcotics, analgesics, antihistamines); bone marrow depression; pregnancy; and in patients with known hypersensitivity to phenothiazines or amitriptyline. Do not give in combination with MAOI drugs because of possible potentiation that may even cause death. Allow at least two weeks between therapies. In such patients therapy with TRIAVIL should be initiated cautiously, with gradual increase in the dosage required to obtain a satisfactory response. Do not give concomitantly with guanethidine or similarly acting compounds since it may block the antihypertensive effect.

WARNINGS: Patients should be warned against driving a car or operating machinery or apparatus requiring alert attention, and that response to alcohol may be increased.

PRECAUTIONS: Suicide is always a possibility in mental depression and may remain until significant remission occurs. Supervise patients closely in case they may require hospitalization or concomitant electroshock therapy. Untoward reactions have been reported after the combined use of antidepressant agents having various modes of activity. Accordingly, consider possibility of potentiation in combined use of antidepressants. Use with caution in patients with glaucoma and those with problems of urinary retention. Perphenazine can lower the convulsive threshold in susceptible individuals. It should be given with caution to patients with convulsive disorders. Dosage of the anticonvulsive agent may have to be increased. Not recommended for use in children. Mania or hypomania may be precipitated in manic-depressives (perphenazine in TRIAVIL seems to reduce likelihood of this effect). If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perpher zine. Caution patients about errors of judgment due change in mood.

ADVERSE REACTIONS: Similar to those reported wi either constituent alone.

Perphenazine: Should not be used indiscriminately. U caution in patients who have previously exhibited seve reactions to other phenothiazines. Likelihood of untowa actions greater with high doses. Closely supervise wi any dosage. Side effects may be any of those report with phenothiazine drugs: extrapyramidal symptor (opisthotonos, oculogyric crisis, hyperreflexia, dyston akathisia, dyskinesia, parkinsonism) usually controlled the concomitant use of effective antiparkinsonian dru and/or by reduction in dosage, but sometimes pers after discontinuation of the phenothiazine; skin disorde (photosensitivity, itching, erythema, urticaria, eczema, to exfoliative dermatitis); other allergic reactions (asthm laryngeal edema, angioneurotic edema, anaphylactoid actions); peripheral edema; reversed epinephrine effec hyperglycemia; endocrine disturbances (lactation, gala torrhea, disturbances of menstrual cycle); altered cer brospinal fluid proteins; paradoxical excitement; EK abnormalities (quinidine-like effect); reactivation of ps chotic processes; catatonic-like states; autonomic rea tions, such as dryness of the mouth, headache, nause vomiting, constipation, obstipation, urinary frequenc blurred vision, nasal congestion, and a change in the pul rate; hypnotic effects; pigmentary retinopathy; corne and lenticular pigmentation; occasional lassitude; musc weakness; mild insomnia. Other adverse reactions r ported with various phenothiazine compounds, but n with perphenazine, include blood dyscrasias (pancyt penia, thrombocytopenic purpura, leukopenia, agranuloc tosis, eosinophilia); liver damage (jaundice, biliary stasis grand mal convulsions; cerebral edema; polyphagia; ph tophobia; skin pigmentation; and failure of ejaculatio Significant unexplained rise in body temperature may su gest intolerance to perphenazine, in which case disco tinue. Antiemetic effect may obscure signs of toxicity d to overdosage of other drugs or make diagnosis of oth disorders such as brain tumors or intestinal obstructi difficult. May potentiate the action of central nervo system depressants (opiates, analgesics, antihistamine barbiturates, alcohol) and atropine. In concurrent the apy with any of these, TRIAVIL should be given in reduce dosage. May also potentiate the action of heat and pho phorous insecticides.

Amitriptyline: Careful observation of all patients reco mended. Side effects include drowsiness (may occ within the first few days of therapy); dizziness; nause excitement; hypertension; fainting; fine tremor; jitte ness; weakness; headache; heartburn; anorexia; i creased perspiration; incoordination; impotenc increased appetite and weight gain; allergic-type rea tions manifested by skin rash, swelling of face and tongu itching; numbness and tingling of limbs, including p ripheral neuropathy; activation of latent schizophren (however, the perphenazine content may prevent this r action in some cases); epileptiform seizures; tempora confusion, disturbed concentration, or transient visu hallucinations on high doses; evidence of anticholiner activity, such as tachycardia, dryness of mouth, stomatit blurring of vision, reversible dilatation of the urinary tra urinary retention, constipation, paralytic ileus; agran locytosis; jaundice. Elderly patients and adolescents c often be managed on lower dosage levels.

For more detailed information, consult your MSD Represe tative or see the package circular. Merck Sharp & Dohm Division of Merck & Co., Inc., West Point, Pa. 19486.

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The actions of the official Tincture and Extract of Belladonna result chiefly from their Atropine content . . . conclude Goodman and Gilman

THE PHARMACOLOGICAL BASIS OF THERAPEUTICS
3rd Edition, page 522

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Antrocol provides the prompt, predictable antisecretory action of the belladonna alkaloid, atropine, fortified with sedation and blended with Bensulfoid, contributing to even absorption.

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Caution: Federal law prohibits dispensing without prescription.

PRESCRIBING INFORMATION

Contraindicated in glaucoma. Use cautiously in prostatic hypertrophy. Side-effects of toxic dose of atropine: flushing, dryness of mouth, cycloplegia, tachycardia and urinary retention.

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Clinical supply available to physicians.

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(fluorouracil)
cream/solution

1/22/68—Treatment with 5% 5-FU cream commences. Patient K.L. showing widespread but mild solar keratoses (also known as actinic keratoses).

for the treatment of solar/actinic keratoses... a topical alternative to conventional therapy

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Efudex®(fluorouracil)—a new alternative to conventional therapy

Efudex presents the physician with a topical alternative to surgery in the treatment of solar or actinic keratoses. It is effective, comparatively inexpensive and especially well-suited for treatment of multiple lesions. Important, too, is the highly desirable cosmetic result. Clinical experience demonstrates that treatment with Efudex results in an extremely low incidence of scarring.*

Highly effective on first and later applications

In clinical trials, depending on the dosage form and strength used, complete involution occurred in 77 to 88 per cent of lesions following treatment. The rate of recurrence was low, ranging from 1.7 to 5.6 per cent up to a year after completion of therapy. When lesions did recur or new ones appeared, repeated courses of Efudex therapy proved effective.*

2/68—After 11 days of treatment. ythema is seen at site of keratoses. In dition, numerous lesions not apparent or to therapy have become manifest sharply defined reactions. Intervening n, also treated, shows no response to rapy.

19/69—One year after cessation of rapy. Skin appears clear with no evi- nce of scarring. Examination reveals k of recurrence or the formation of w lesions.

Predictable sequence of therapeutic response

Two to four weeks constitutes a typical course of Efudex therapy. The response is usually characteristic and predictable. After three or four days of treatment, erythema begins to appear in the area of the keratoses. This is followed by an intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of the inflammatory reaction generally occurs two weeks after the start of therapy, and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. A mild erythema may remain for two to three months before gradually receding.

Selective—with a high degree of safety

Despite the temporary unsightliness and discomfort of the inflammatory episode, Efudex is, in general, more readily tolerated than surgery. Clinical work shows the intense inflammatory response to be limited to the area of the lesion. Normal skin is not similarly affected. Another measure of Efudex safety: systemic absorption of topical fluorouracil was insignificant, indicating a low risk of systemic toxicity.*

Two strengths—two convenient dosage forms

Efudex is available as a 2% or 5% solution or as a 5% cream. It is applied twice daily by the patient with a nonmetal applicator or suitable glove.

Before prescribing Efudex, however, there are two important considerations. First, please consult the complete prescribing information for precautions, warnings and adverse reactions. Second, advise the patient that treated lesions should respond with the characteristic but transient inflammation. A positive sign that Efudex is working for them.

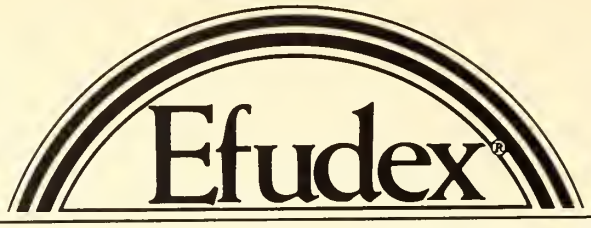
*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

2% and 5% Solutions; 5% Cream Applied twice daily—resolves solar or actinic keratoses.

new
Efudex®
(fluorouracil)
cream/solution

For full prescribing information, please see the following page.

Roche introduces



(fluorouracil) cream/solution the new standardized topical for solar/actinic keratoses

Description: Efudex solutions and cream are topical preparations containing the fluorinated pyrimidine 5-fluorouracil, an antineoplastic antimetabolite.

Efudex Solution consists of 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris-(hydroxymethyl) aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Efudex Cream contains 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

Actions: There is evidence that the metabolism of fluorouracil in the anabolic pathway blocks the methylation reaction of deoxyuridylic acid to thymidylic acid. In this fashion fluorouracil interferes with the synthesis of deoxyribonucleic acid (DNA) and to a lesser extent inhibits the formation of ribonucleic acid (RNA). Since DNA and RNA are essential for cell division and growth, the effect of fluorouracil may be to create a thymine deficiency which provokes unbalanced growth and death of the cell. The effects of DNA and RNA deprivation are most marked on those cells which grow more rapidly and which take up fluorouracil at a more rapid pace. The catabolic metabolism of fluorouracil results in degradative products (*e.g.*, CO_2, urea, α-fluoro-β-alanine) which are inactive.

Studies in man with topical application of ^{14}C-labeled Efudex demonstrated insignificant absorption as measured by ^{14}C content of plasma, urine and respiratory CO_2.

Indications: Efudex is recommended for the topical treatment of multiple actinic or solar keratoses.

Contraindications: Efudex is contraindicated in patients with known hypersensitivity to any of its components.

Warnings: If an occlusive dressing is used, there may be an increase in the incidence of inflammatory reactions in the adjacent normal skin.

Prolonged exposure to ultraviolet rays should be avoided while under treatment with Efudex because the intensity of the reaction may be increased.

Usage in Pregnancy: Safety for use in pregnancy has not been established.

Precautions: If Efudex is applied with the fingers, the hands should be washed immediately afterward. Efudex should be applied with care near the eyes, nose and mouth. To rule out the presence of a frank neoplasm, a biopsy should be made of those areas failing to respond to treatment or recurring after treatment.

Adverse Reactions: The most frequently encountered local reactions were pain, pruritus, hyperpigmentation and burning a the site of application. Other local reactions included dermatitis scarring, soreness and tenderness.

Also reported were insomnia, stomatitis, suppuration, scaling swelling, irritability, medicinal taste, photosensitivity and lacrimation.

Laboratory abnormalities reported were leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Efudex should be applied twice dail with a nonmetal applicator or suitable glove in an amount of th solution or cream sufficient to cover the lesion. When Efudex is applied to a lesion, a response occurs with the following sequen erythema, usually followed by vesiculation, erosion, ulceration, necrosis and epithelization. The lower frequency and intensity c activity in adjacent normal skin indicate a selective cytotoxic property. Medication should be continued until the inflammatory reaction reaches the erosion, necrosis and ulceration stage, at which time use of the drug should be terminated. The usual duration of therapy is from 2 to 4 weeks. Complete healing of the lesion may not be evident for 1 to 2 months following cessation o Efudex therapy.

How Supplied: Efudex Solution, 10-ml drop dispensers—containi 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Efudex Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

Clinical Studies: The effectiveness of the three preparations as determined by complete involution of solar keratoses was: 2% Solution, 77% of 282 lesions; 5% Solution, 88% of 202 lesions; and 5% Cream, 85% of 189 lesions. In those lesions wher complete involution followed treatment, the rate of possible recurrences observed clinically at periods up to 12 months or mor was: 2% Solution, 4.6% of 218 lesions; 5% Solution, 1.7% of 177 lesions; and 5% Cream, 5.6% of 160 lesions. Because of the toxic potential of fluorouracil, some physicians preferred to use the 2% solution when large areas were to be treated. Approximately 30% of the lesions required treatment for two weeks or less; approximately 78% required four weeks or less for adequate treatment.

Division of Hoffmann-La Roche Inc.
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Precautions: Administer with caution to patients with incipient glaucoma, bladder neck obstruction or urinary bladder atony. Prolonged use of barbiturates may be habit-forming.
Side effects: Blurred vision, dry mouth, dysuria, and other atropine-like side effects may occur at high doses, but are only rarely noted at recommended dosages.
Dosage: Adults: One or two tablets three or four times daily. Dosage can be adjusted depending on diagnosis and severity of symptoms. Children 2 to 12 years: One half or one tablet three or four times daily. Tablets may be chewed or swallowed with liquids.

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to move,
and the Latin **sedatus**,
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traindications: Hypersensitivity to any ponent.

ning: In renal impairment, since liver toxi is possible, lower doses are indicated; dur prolonged therapy consider serum level rminations. Photodynamic reaction to sun t may occur in hypersensitive persons. osensitive individuals should avoid expo; discontinue treatment if skin discomfort irs.

autions: Drowsiness, anorexia, slight gas distress can occur. In excessive drowsi, consider longer dosage intervals. Persons on full dosage should not operate vehicles. Nonsusceptible organisms may overgrow; treat superinfection appropriately. Treat beta-hemolytic streptococcal infections at least 10 days to help prevent rheumatic fever or acute glomerulonephritis. Tetracycline may form a stable calcium complex in bone-forming tissue and may cause dental staining during tooth development (last half of pregnancy, neonatal period, infancy, early childhood).

Adverse Reactions: *Gastrointestinal*—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. *Skin*—maculopapular and erythematous rashes; exfoliative dermatitis; photosensitivity; onycholysis, nail discoloration. *Kidney*—dose-related rise in BUN. *Hypersensitivity reactions*—urticaria, angioneurotic edema, anaphylaxis. *Intracranial*—bulging fontanels in young infants. *Teeth*—yellow-brown staining; enamel hypoplasia. *Blood*—anemia, thrombocytopenic purpura, neutropenia, eosinophilia. *Liver*—cholestasis at high dosage.

Upon adverse reaction, stop medication and treat appropriately.

ederle LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York 10965

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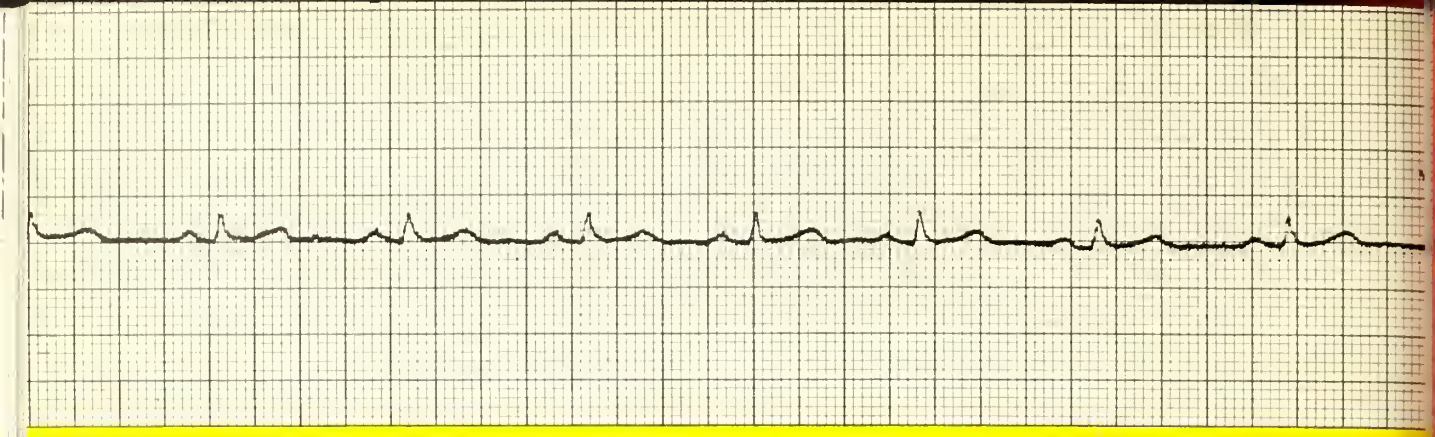

When disease is ruled out and psychic tension is implicated

Valium® (diazepam)

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms have occurred following abrupt discontinuance. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation, have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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THE JOURNAL
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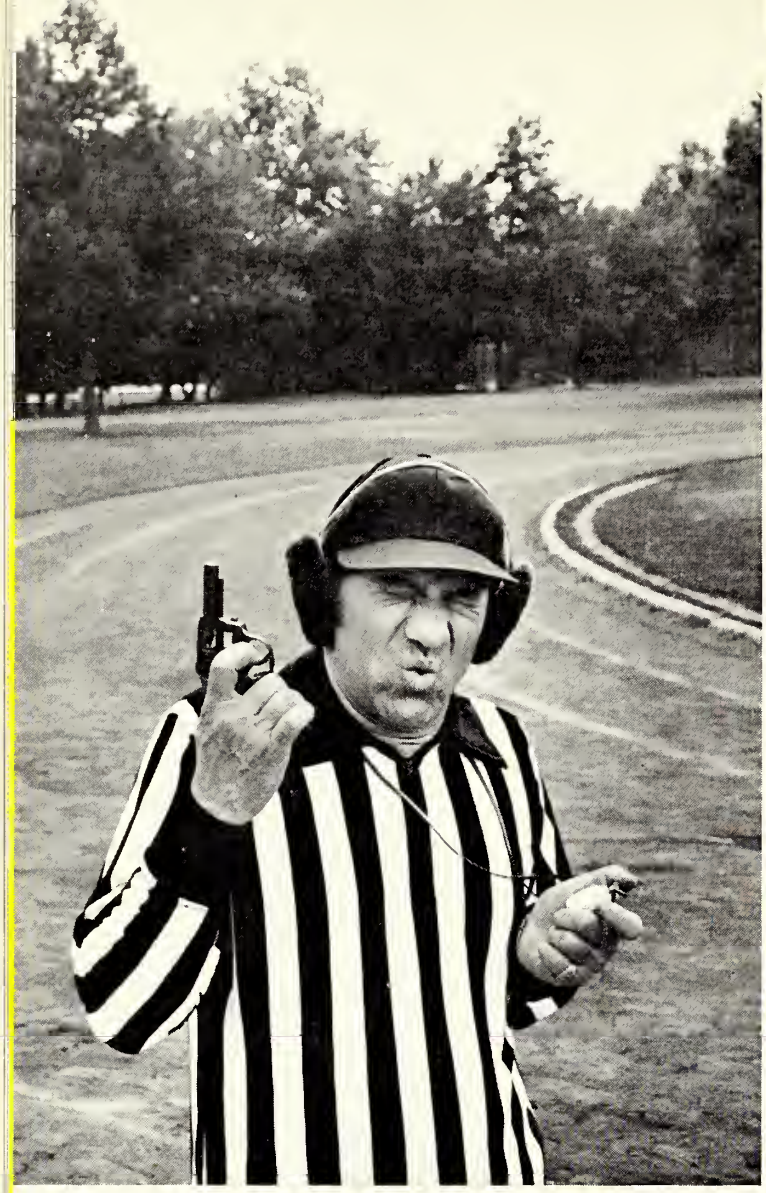

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References: 1. Batterman, R. C., and Grossman, A. J.: Fed. Proc. *14*:316, 2. Goodman, L. S., and Gilman, A., ed.: The Pharmacological Basis of T peutics, ed. 3. New York, The Macmillan Company, 1965, p. 331. 3. Kestl C., and Gyurik, J.: Industr. Med. *31*:372, 1962. 4. Forster, S., *et al.*: A J. Orthop. *2*:285, 1960. 5. Friend, D Clin. Pharmacol. Ther. *5*:871, 1964.

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(1) Siver, R. H.: CMD, 21:109, September 1954. (2) Frykman, H. H.: Minn. Med., 38:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., 51:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., 15:15-16, October 1965. (5) Weekes, D. J.: NY State Jour. Med., 58:2672-2673, August 1958. (6) Ellis, S. and Spratt, J. S.: JOUR. AMER. GER. SOC., 18:410-415, May 1970.

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* PATRICIA A. BERGERON, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., will be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.
Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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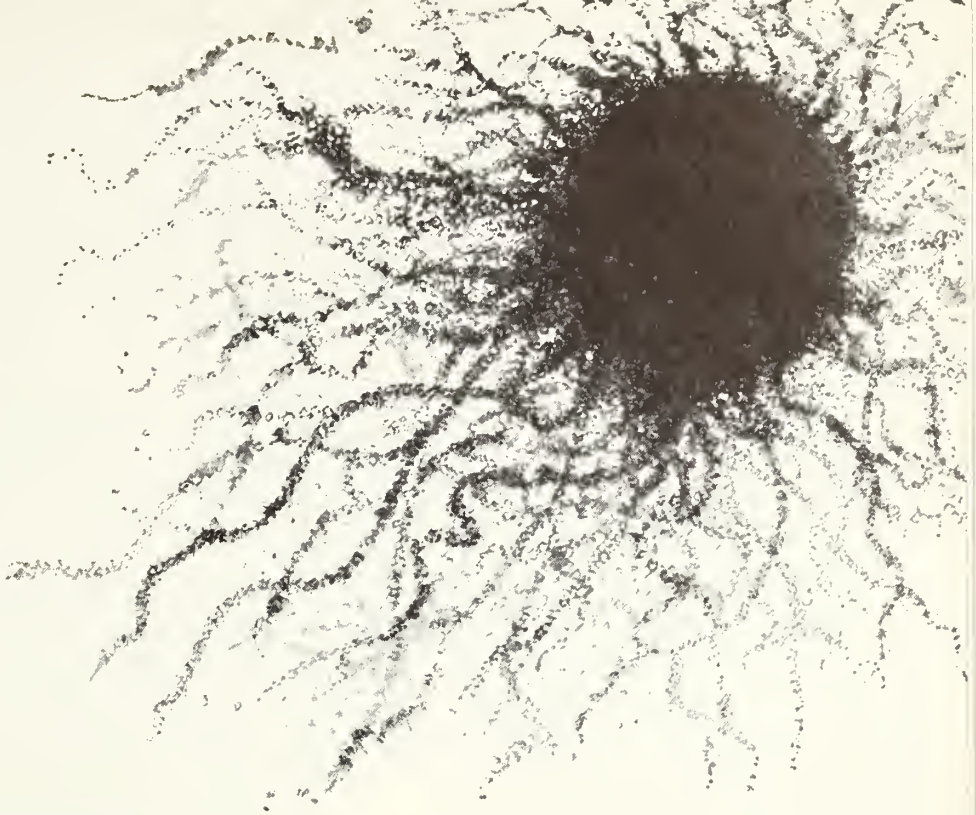

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*Slanger, A.: Med. Times *94*:150 (Feb.) 1966.

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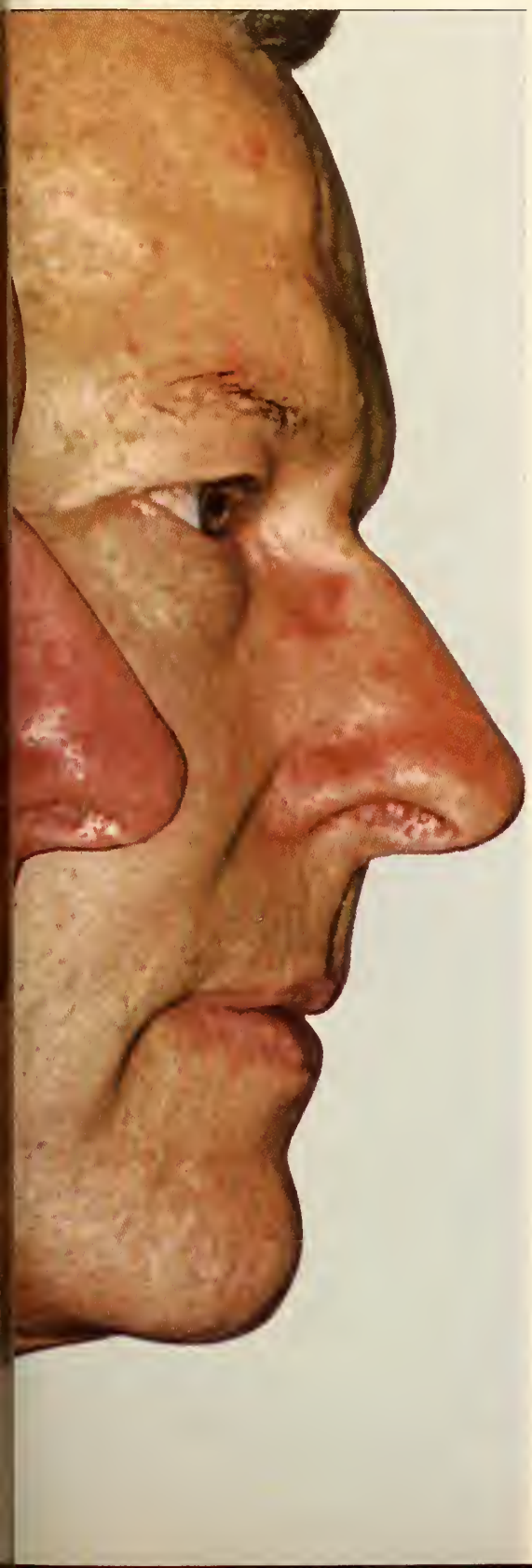
1/22/68—Treatment with 5% 5-FU cream commences. Patient K.L. showing widespread but mild solar keratoses (also known as actinic keratoses).

/2/68—After 11 days of treatment. rythema is seen at site of keratoses. In ddition, numerous lesions not apparent rior to therapy have become manifest y sharply defined reactions. Intervening kin, also treated, shows no response to ıerapy.

/19/69—One year after cessation of ıerapy. Skin appears clear with no evi- ence of scarring. Examination reveals ıck of recurrence or the formation of ew lesions.



Predictable sequence of therapeutic response

Two to four weeks constitutes a typical course of Efudex therapy. The response is usually characteristic and predictable. After three or four days of treatment, erythema begins to appear in the area of the keratoses. This is followed by an intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of the inflammatory reaction generally occurs two weeks after the start of therapy, and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. A mild erythema may remain for two to three months before gradually receding.

Selective—with a high degree of safety

Despite the temporary unsightliness and discomfort of the inflammatory episode, Efudex is, in general, more readily tolerated than surgery. Clinical work shows the intense inflammatory response to be limited to the area of the lesion. Normal skin is not similarly affected. Another measure of Efudex safety: systemic absorption of topical fluorouracil was insignificant, indicating a low risk of systemic toxicity.*

Two strengths—two convenient dosage forms

Efudex is available as a 2% or 5% solution or as a 5% cream. It is applied twice daily by the patient with a nonmetal applicator or suitable glove.

Before prescribing Efudex, however, there are two important considerations. First, please consult the complete prescribing information for precautions, warnings and adverse reactions. Second, advise the patient that treated lesions should respond with the characteristic but transient inflammation. A positive sign that Efudex is working for them.

*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

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Efudex Cream contains 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

Actions: There is evidence that the metabolism of fluorouracil in the anabolic pathway blocks the methylation reaction of deoxyuridylic acid to thymidylic acid. In this fashion fluorouracil interferes with the synthesis of deoxyribonucleic acid (DNA) and to a lesser extent inhibits the formation of ribonucleic acid (RNA). Since DNA and RNA are essential for cell division and growth, the effect of fluorouracil may be to create a thymine deficiency which provokes unbalanced growth and death of the cell. The effects of DNA and RNA deprivation are most marked on those cells which grow more rapidly and which take up fluorouracil at a more rapid pace. The catabolic metabolism of fluorouracil results in degradative products (*e.g.*, CO_2, urea, α-fluoro-β-alanine) which are inactive.

Studies in man with topical application of ^{14}C-labeled Efudex demonstrated insignificant absorption as measured by ^{14}C content of plasma, urine and respiratory CO_2.

Indications: Efudex is recommended for the topical treatment of multiple actinic or solar keratoses.

Contraindications: Efudex is contraindicated in patients with known hypersensitivity to any of its components.

Warnings: If an occlusive dressing is used, there may be an increase in the incidence of inflammatory reactions in the adjacent normal skin.

Prolonged exposure to ultraviolet rays should be avoided while under treatment with Efudex because the intensity of the reaction may be increased.

Usage in Pregnancy: Safety for use in pregnancy has not been established.

Precautions: If Efudex is applied with the fingers, the hands should be washed immediately afterward. Efudex should be applied with care near the eyes, nose and mouth. To rule out the presence of a frank neoplasm, a biopsy should be made of those areas failing to respond to treatment or recurring after treatment.

Adverse Reactions: The most frequently encountered local reactions were pain, pruritus, hyperpigmentation and burning at the site of application. Other local reactions included dermatitis, scarring, soreness and tenderness.

Also reported were insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity and lacrimation.

Laboratory abnormalities reported were leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Efudex should be applied twice daily with a nonmetal applicator or suitable glove in an amount of the solution or cream sufficient to cover the lesion. When Efudex is applied to a lesion, a response occurs with the following sequence: erythema, usually followed by vesiculation, erosion, ulceration, necrosis and epithelization. The lower frequency and intensity of activity in adjacent normal skin indicate a selective cytotoxic property. Medication should be continued until the inflammatory reaction reaches the erosion, necrosis and ulceration stage, at which time use of the drug should be terminated. The usual duration of therapy is from 2 to 4 weeks. Complete healing of the lesion may not be evident for 1 to 2 months following cessation of Efudex therapy.

How Supplied: Efudex Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Efudex Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

Clinical Studies: The effectiveness of the three preparations as determined by complete involution of solar keratoses was: 2% Solution, 77% of 282 lesions; 5% Solution, 88% of 202 lesions; and 5% Cream, 85% of 189 lesions. In those lesions where complete involution followed treatment, the rate of possible recurrences observed clinically at periods up to 12 months or more was: 2% Solution, 4.6% of 218 lesions; 5% Solution, 1.7% of 177 lesions; and 5% Cream, 5.6% of 160 lesions. Because of the toxic potential of fluorouracil, some physicians preferred to use the 2% solution when large areas were to be treated. Approximately 30% of the lesions required treatment for two weeks or less; approximately 78% required four weeks or less for adequate treatment.

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Volume Sixty-one | Brunswick, Maine, November 1970 | Number 11

A Method of Treating Sciatic Pain

HOWARD P. SAWYER, JR., M.D.*

Pain along the course and distribution of the sciatic nerve (i.e., buttock, posterior thigh, postero-laterally in the leg, into the lateral border of the foot) has long been defined as sciatica. Although the diagnosis of sciatica is usually not a difficult one to make, identification of the specific etiology is more difficult. The causes are numerous including many pathological processes which may involve the spinal cord, nerve roots and their ganglia, lesions of the lumbar or sacral nerves, and lesions of the sciatic nerve or branches thereof. A radiculitis may be related to septic foci, to injected foreign material, to virus diseases, or to metabolic or nutritional disturbances. Other causes include extradural adhesions which may follow surgery or intradural adhesions from trauma or myelography.

Although all these possibilities must be kept in mind, patients referred by neurosurgeons or orthopedists will generally have a history of one or more laminectomies for removal of a ruptured intervertebral disc. The commonest working diagnosis for the consulting anesthesiologist is "post laminectomy pain, etiology undetermined."

The intervertebral disc consists of an elastic fibrocartilaginous envelope, the annulus fibrosus, containing within it the mucoid or gelatinous nucleus pulposus. Either by attrition, degeneration or trauma the cartilage tears. The nucleus, which in middle life is contained under a pressure of thirty pounds,[1] is thus forced to the periphery of the annulus, producing a bulge against the posterior longitudinal ligament. Due to its inherent strength and firm attachment to the posterior aspect of the vertebral bodies this ligament usually forces the bulge laterally, causing pressure on the nerve roots as they descend in the spinal canal. If the nuclear material ruptures through the annulus, adhesions may form between nerve root and the nucleus or between nerve root and ligamentum flavum.

By biopsy of the dorsal root in patients with nerve compression, Lindahl and Rexed[2] demonstrated a 70% incidence of edema and infiltration of the root by lymphocytes. Irsegler[3] reported enlarged intraneural vessels with infiltration by lymphocytes and histiocytes in an inadvertently resected lumbar root that had been compressed for six months by an intervertebral disc. Furthermore, the nerve sleeve, like other tissues, will frequently show adhesions following hemorrhage and trauma. In the course of a laminectomy for removal of a protruded disc, epidural fat which is traumatized or removed is likely also to be replaced by fibrous tissue with immobilization or severe limitation of the normal excursion of the nerve. Chronic arachnoiditis with significant sciatic pain presumably due to irritation from the contrast media has been reported following myelography for the investigation of suspected lesions at the cervical level.

Patients with chronic low back pain and lumbosacral radiation (sometimes referred to as the "lumbosciatic syndrome") due to a herniated nucleus pulposus may have associated pathological changes which are not corrected by the removal of the protruded portion of the disc.[13] These may include subluxed articular facets with stretched joint capsules and degenerative joint changes which probably account for the persistence of the back pain even when the leg pain is greatly improved.

Therapeutic measures aimed at relieving the pain of sciatica are as numerous as the etiologic possibilities. Many of these such as heat, rest, immobilization, physical therapy, deep roentgen therapy, muscle relaxants, analgesics, and anti-inflammatory drugs will have been tried and found relatively ineffective by the time these patients have consulted various specialists before reaching the anesthesiologist.

In the late nineteenth century shortly following August Bier's description of spinal analgesia, several French physicians had employed it for the relief of lumbar and sciatic neuralgia.[5] In 1901, Sicard[6] and Cathelin[7] independently described the injection of substances into the

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epidural space via the sacral hiatus. Dissatisfied with the high incidence of headache and vomiting that followed subarachnoid cocaine used to treat sciatica, Sicard injected it in low concentrations with saline into the epidural space with good results.

Later, lysis of adhesions became a primary goal, and those who used rapid massive fluid injections into the epidural space for this purpose felt that volumes of fifty to one hundred ml. should be used.[8] This frequently produced considerable pain, headache, dizziness and occasionally shock presumably due to the excruciating pain of the rapid injection, exaggeration of the sciatic pain from sudden freeing of the adhesions and/or compression of the subarachnoid space, spinal cord and nerve roots. Kelman[9] substituted ¾% metycaine for saline to decrease the pain of injection and to break the vicious cycle of pain and muscle spasm, thus producing longer periods of freedom from pain.

Evans[10] felt that smaller volumes were sufficient as did Goelbert[11] who used thirty ml. of procaine with hydrocortisone followed by passive straight leg raising to further the neurolysis. Sehgal and Gardner[12] found that some patients who did not respond to epidural procaine and steroid obtained relief from the subarachnoid injection of procaine and methylprednisolone acetate, particularly those who had undergone previous Pantopaque myelography.[13] However, tuberculous meningitis has been reported following this form of therapy by Roberts et al.[14] Smith and Brown[15] have reported some success in patients not responsive to other measures following the injection into the intervertebral disc of chymopapain, the major proteolytic enzyme of papaya latex, presumably by enzymatic dissolution of the disc.

An excellent description of the anatomy of the sacrum, sacral canal, and epidural space with helpful practical suggestions for the technique of caudal injection has been provided by Southworth and Hingson.[16] They point out that due to the fibrous curtain over the intervertebral foramina, fluid injected into the epidural space must infiltrate into the nerve roots or pass through the connective tissue network into the paravertebral space in order to produce effects.

That pain relief does not require the use of local anesthetics has been demonstrated not only by the perineural injection of pitcher plant distillate, which produces relief of neuralgia without any local anesthesia, but also by several studies in which the peridural injection of saline alone was employed to relieve sciatica.[8,9,10] The concentration of cocaine used by Sicard[5] for this same purpose was so low no cutaneous analgesia was produced. The mechanism of this pain relief with normal saline alone is not clearly understood. Pressure on nerve roots is known to impair their function. A sudden rise in pressure caused by the rapid injection of saline into the peridural or subarachnoid space frequently provides sufficient analgesia to facilitate passive leg exercises (either straight leg raising or flexion at the hip with extension at the knee) which would otherwise be extremely painful. The ultimate relief of pain would appear to result mainly from the breakup of fibrous adhesions or stretching of the nerve roots by the pressure of the injected solutions facilitated by the passive streching. The duration of pain relief may depend on the effectiveness of the corticosteroid in preventing further adhesions.[11]

Method

Between 1 January 1961 and 1 July 1970, 167 patients were seen in consultation by members of the anesthesia department of the Maine Medical Center for assistance in the management of lumbosciatic pain. Treatment was predicted on the assumption that in the majority of these patients pain was largely caused by periradicular adhesions or scarring. Of these, 155 had previously undergone lumbar laminectomy and/or spinal fusion.

After obtaining a history, reviewing the record, and examining the patient an injection of 25-30 ml. of a 1% solution of either procaine, lidocaine, chlorprocaine, or mepivicaine with hydrocortisone 100 mg., dexamethasone 4 mg., or methyl prednisolone 40 mg. was made via the sacral hiatus into the epidural space. The first portion of the injection was made slowly and the balance injected as rapidly as the patient would tolerate, which was extremely variable. This was followed in ten to twenty minutes by passive straight leg raising and hip flexion with knee extension to aid further in lysing any adhesions. Blood pressure and pulse date were monitored until stable. Patients were instructed to remain horizontal for two hours and then to assume the vertical position gradually by stages to minimize cerebral ischemia which might result from a sudden shifting of blood into the vasodilated lower extremities.

Although the injections were frequently painful, complications were rarely encountered. Several patients complained briefly of mild dizziness; two showed signs of an inadvertent subarachnoid injection, one with hypotension necessitating the use of a vasopressor. In only two instances was it felt that the sacrum prevented satisfactory entry into the epidural space so that a lumbar epidural approach was required. This approach was otherwise used infrequently, when pain relief was not obtained from the sacral approach in patients who demonstrated definite signs of nerve root irritation.

Initially this treatment was limited to inpatients and hydrocortisone was the steroid used. Later outpatients were accepted, provided they would be driven home by someone else. Dexamethasone phosphate also became the steroid of choice for its reported greater anti-inflammatory effect. The caudal blocks and exercises were done daily or on alternate days, the number of injections in a single series varying from two to five although most consisted of three. Two patients received four such series of blocks, three had three, fifteen had two, and 147 underwent a single series. A total of 194 series of epidural injections were administered to 167 patients. In 1969, methyl prednisolone acetate suspension was

TABLE 1

AGE AND SEX DISTRIBUTION

Age	*20-29*	*30-39*	*40-49*	*50-59*	*60-69*	*over 70*
Men	12	29	36	13	10	4
Women	5	9	18	9	9	0

TABLE 2

ETIOLOGY OF SCIATIC PAIN

Diagnosis	*Series of Blocks*
Adhesions	45
Etiology unknown	27
Etiology unknown with big psychic overlay	16
Unstable back	10
Recurrent disc	9
Arachnoiditis	8
Spondylosis	4
Arthritis	4
	123

TABLE 3

CLASSIFICATION OF RESULTS WITH HYDROCORTISONE

	Physician Evaluation					*Patient Evaluation*			
Diagnosis	*E*	*G*	*F*	*P*	*Series*	*E*	*G*	*F*	*P*
Adhesions	5	1	0	1	7	4	2	0	1
Etiology Unknown	2	0	1	4	7	2	2	1	2
Etiology Unknown with Overlay	1	0	0	1	2	0	0	1	1
Unstable Back	0	1	0	2	3	0	1	0	2
Recurrent Disc	1	0	1	0	2	1	0	0	1
Arachnoiditis	0	0	0	2	2	0	0	0	2
Spondylosis	—	—	—	—	0	—	—	—	—
Arthritis	1	0	0	1	2	1	0	1	0
	10	2	2	11	25	8	5	3	9

used for its prolonged local contact and the interval between blocks was increased to a week.

RESULTS

Questionnaires were sent to 165 (111 male and 54 female) patients who had been thus treated. Answers were obtained either by mail or telephone follow-up from 102 or 61.8%, representing 123 separate series of blocks. Hospital and outpatient records were reviewed to establish for all the number of caudal blocks done, drugs used, immediate results, and on those who replied to obtain a diagnosis and any available evidence to corroborate the results. The average age of the males was 45 and of the females 46 years. The distribution by age groups based on available information is shown in Table 1.

Review of the charts led to a wide variety of recorded diagnoses including recurrent ruptured disc, arthritis, arthritis with scarring, traumatic arthritis, peridural scarring, adhesions with large psychogenic component, unstable back, unstable back with scarring, radiculopathy with adhesions, postlaminotomy pain with psychogenic overlay, spondylosis, spondylosis with conversion, etiology unknown, etiology unknown with psychic contribution. To unscramble such a variety of diagnoses and draw some reasonably valid conclusions concerning the results of the treatment appeared to be an overwhelming task. Table 2 indicates the classification finally selected.

TABLE 4

CLASSIFICATION OF RESULTS WITH DEXAMETHASONE

	Physician Evaluation					*Patient Evaluation*			
Diagnosis	*E*	*G*	*F*	*P*	*Series*	*E*	*G*	*F*	*P*
Adhesions	8	2	3	22	35	8	2	12	13
Etiology Unknown	7	2	1	3	13	3	5	3	2
Etiology Unknown with Overlay	1	0	2	9	12	1	0	2	9
Unstable Back	2	0	0	2	4	1	0	1	2
Recurrent Disc	0	0	0	7	7	0	0	2	5
Arachnoiditis	1	1	0	1	3	2	0	0	1
Spondylosis	1	1	0	2	4	2	0	1	1
Arthritis	0	0	0	1	1	0	0	1	0
	20	6	6	47	79	17	7	22	33

TABLE 5

CLASSIFICATION OF RESULTS WITH METHYL PREDNISOLONE

	Physician Evaluation					*Patient Evaluation*			
Diagnosis	*E*	*G*	*F*	*P*	*Series*	*E*	*G*	*F*	*P*
Adhesions	0	0	0	3	3	0	0	2	1
Etiology Unknown	0	1	0	6	7	1	0	2	4
Etiology Unknown with Overlay	0	0	1	1	2	1	0	0	1
Unstable Back	0	1	0	2	3	0	1	0	2
Recurrent Disc	—	—	—	—	0	—	—	—	—
Arachnoiditis	0	0	0	3	3	0	0	0	3
Spondylosis	—	—	—	—	0	—	—	—	—
Arthritis	0	0	0	1	1	0	0	0	1
	0	2	1	16	19	2	1	4	12

Adhesions comprised 36% of the causes listed which is comparable to the observations at re-exploration reported by Greenwood, McGuire, and Kimbell.[17]

The questionnaire provided several choices in percentage of both leg and back pain relieved, several choices for duration of relief, and a one word description (excellent, good, fair, poor) for the patients to indicate their impressions of the results as well as an opportunity to make any desired comment. For purposes of tabulating the many combinations the following criteria were selected.

Excellent	80-100% relief for over one year
Good	70-100% relief for over six months
Fair	Over 60% relief for less than six months
Poor	Any degree of relief lasting less than three months

Tables 3, 4, and 5 represent the results obtained with the different steroids as classified by the patients and by the author using the above noted criteria, which although somewhat arbitrary, would appear to correlate closely with the patients' own evaluations. It was felt that there was insufficient difference in the actions of lidocaine, mepivicaine, procaine, and chlorprocaine to

TABLE 6

OVERALL RESULTS

	Physician Evaluation					Patient Evaluation			
Diagnosis	*E*	*G*	*F*	*P*	*No. Series*	*E*	*G*	*F*	*P*
Adhesions	13	3	3	26	45	12	4	14	15
Etiology Unknown	9	3	2	13	27	6	7	6	8
Etiology Unknown with Overlay	2	0	3	11	16	2	0	3	11
Unstable Back	2	2	0	6	10	1	2	1	6
Recurrent Disc	1	0	1	7	9	1	0	2	6
Arachnoiditis	1	1	0	6	8	2	0	0	6
Spondylosis	1	1	0	2	4	2	0	1	1
Arthritis	1	0	0	3	4	1	0	2	1
	30	10	9	74	123	27	13	29	54

TABLE 7

RELIEF OF BACK PAIN AS EVALUATED BY PATIENTS

Diagnosis	*Exc.-Good*	*Fair-Poor*
Adhesions	11	24
Etiology Unknown	6	12
Etiology ? Overlay	4	9
Unstable back	1	6
Recurrent disc	2	7
Arachnoiditis	4	3
Spondylosis	0	1
Arthritis	2	1
	30	63

break down the results by the local anesthetic used. With the breakdown by steroids alone, the number of cases in many categories is too small to warrant any conclusions.

With hydrocortisone, twelve had good or excellent results or 48% of the total series of 25 with 86% good or excellent results in seven patients diagnosed as having pain due to adhesions.

The overall results with dexamethasone indicate a combined good and excellent relief of pain in 26 of 79 patients or 33%, with the best results in those with arachnoiditis or pain of unknown etiology. Those with unstable backs or spondylosis had 50% good or excellent results, again of limited statistical value however, due to the small number of cases.

There were no excellent results in any etiologic category treated with methylprednisolone, and the total of good results was only two out of nineteen or 10.5%. To draw any conclusions from this small group would be premature.

Combining all groups, the overall 40 good or excellent results out of 123 series of caudal blocks produced a 32% favorable result. This is shown in Table 6.

Back pain was not present in all patients, but of the 93 who did indicate back pain as a part of their problem, 30 or 32% had good or excellent relief of their back pain. Table 7 indicates the results by individual diagnoses.

Lest the anesthesiologist consider himself the last resort in some of these pain problems, it should be pointed out that 33 patients had further operations which provided good relief of pain in 20 as shown in Table 8.

TABLE 8

PATIENTS RECEIVING FURTHER SURGERY

Diagnosis	*Pain relief*	*No relief*
Adhesions	6	5
Etiology Unknown	1	5
Recurrent disc	5	1
Unstable back	5	0
Arachnoiditis	2	1
Arthritis	1	0
Spondylosis	0	1
	20	13

TABLE 9

RESULTS OF OTHER EPIDURAL INJECTION FOR SCIATICA

		E	*G*	*F*	*P*	*Total*	*E-G%*
Goelbert et al[11]	1960		137	21	81	239	57%
Kelman[9]	1949	49	45	17	5	116	81%
Southworth[16]	1943		15			21	71%
Bhata[8]	1966	6	9	1	2	18	83%
Sawyer	1970	30	10	9	74	123	33%

COMMENT

This report suffers from the usual problems of a retrospective study. The treatments were given by several members of one department without the advantage of a recorded protocol so that valuable information was frequently not available. There was, for example, a clinical impression that patients who showed neither limitation of straight leg raising nor significant discomfort on injection as a group obtained much less pain relief. This could not be confirmed for lack of recorded information. Information was similarly unavailable as to the number of patients who, at the time of the first caudal block, experienced analgesia in the leg opposite to the painful one. This contralateral analgesia occurred frequently and was felt to be due to adhesions blocking the movement of solution through the foramina on the painful side.

The questionnaire was returned only by 62% of the patients treated, some of whom failed to answer all the questions. Review of both in- and out-patient records created an impression that many diagnoses were recorded with understandable uncertainty.

Different authors may use varied criteria for classifying their results in treating sciatica with epidural injections. Table 9 represents an effort to correlate results of some other studies.

SUMMARY

Some of the stages leading to a current concept in the management of "post laminotomy lumbo-sciatic pain" have been briefly described. The results of a treatment consisting of peridural injection via the sacral hiatus of combinations of local anesthetic and steroids followed by passive straight leg raising have been presented and compared with other reported results.

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Bacteremic Consumptive Coagulopathy

WILLIAM J. HALL, III, M.D.*

ABSTRACT

Two instances of presumed bacteremic consumptive coagulopathy were noted among 76 consecutive episodes of Gram negative bacteremia during 1965 and 1966 at University Hospital, Boston, Massachusetts. The apparent incidence of this complication was 2.6% among patients retrospectively studied. Such a low incidence probably does not represent the true rate of occurrence of Gram negative bacteremic consumptive coagulopathy and indicates the need for prospective examination of a large number of patients likely to experience Gram negative septicemia.

INTRODUCTION

The liberation of small amounts of bacterial cell wall lipopolysaccharide into the vascular compartments of animals and man is known to initiate intravascular coagulation and to deplete whole blood of platelets and of plasma clotting factors. Consumptive coagulopathy has been described in patients with Gram negative bacteremia[1,2,3] and in human infections caused by two species of Rickettsiae.[4,5,6] Thrombocytopenia complicating Gram positive coccal septicemia has been documented.[7] Intravascular coagulation has been noted to complicate arbovirus infection, yellow fever and the hemorrhagic fevers of Asia and of South America.[8] Acute falciparum malaria in humans and experimental simian malaria have both been shown to deplete whole blood of clotting factors and platelets.[9]

The incidence of consumptive coagulopathy in Gram negative septicemia and its role, if any, in the pathogenesis of Gram negative bacteremic shock are not known. Two episodes of bacteremic consumptive coagulopathy occurring at University Hospital, Boston, Massachusetts, comprise the present report and constitute a crude assessment of the incidence of this disorder in Gram negative bacteremia.

PATIENTS AND METHODS

The charts of all patients who experienced septicemia at University Hospital during the 24 months from January 1, 1965 to December 31, 1966 were examined. Seventy-six episodes of blood stream invasion by Gram nega-

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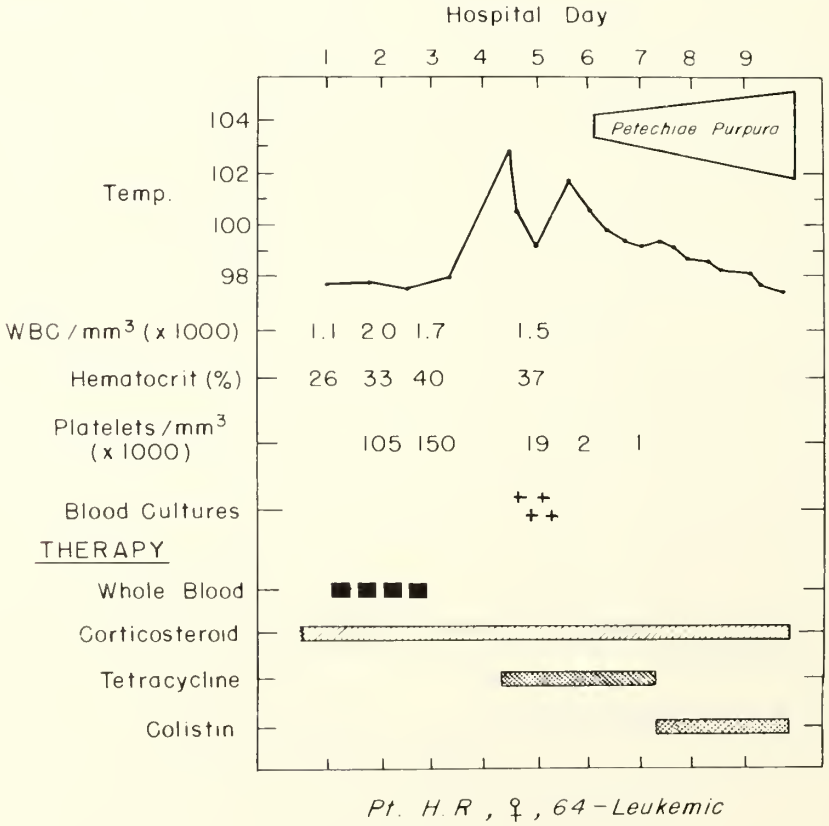

Fig. 1

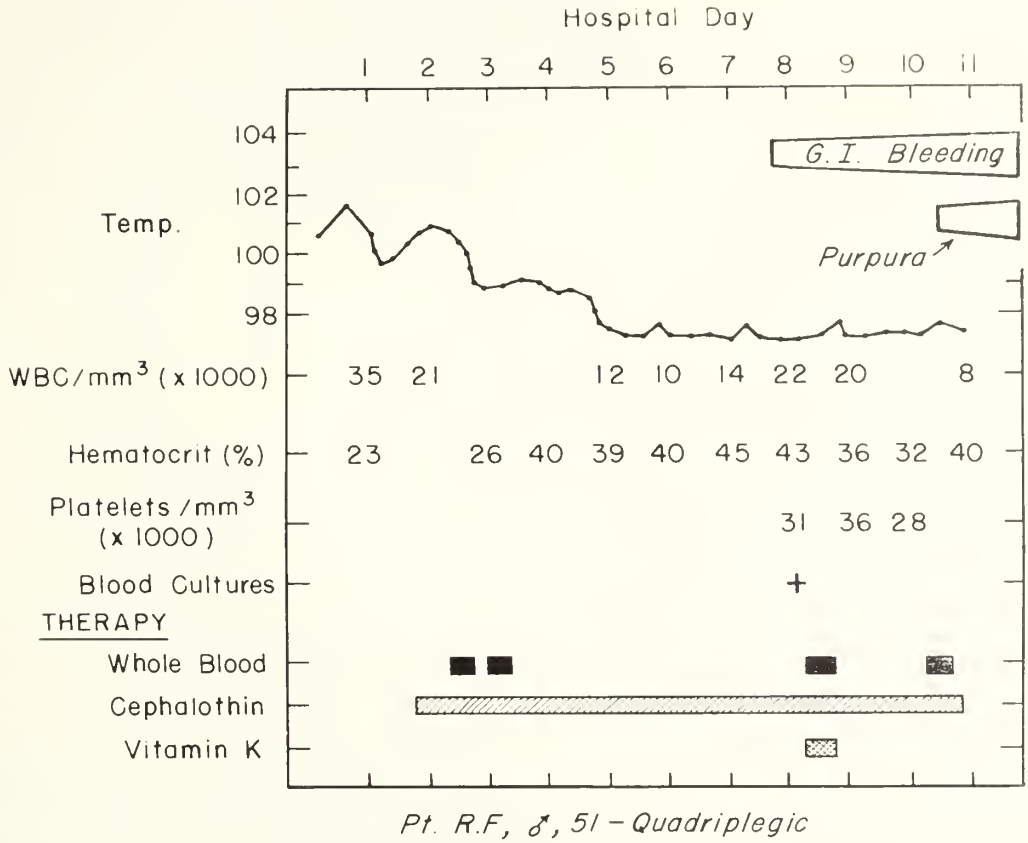

Fig. 2

tive bacilli were encountered among 139 episodes of septicemia. Two of 76 patients (2.6%) demonstrated clinical stigmata of a newly-acquired bleeding disorder during the course of bacteremia.

Coagulation studies were performed by Lilia Talerico, M.D., Section of Hematology, University Hospital, Boston, Massachusetts, according to standard hematological procedures.

Case Reports

Case 1: H. R., (Fig. 1.), a 64-year-old white female was admitted to University Hospital in September 1966. In 1955, lymphatic leukemia had been diagnosed and the patient had subsequently received two courses of nitrogen mustard (in 1958 and in 1962). Platelet counts performed during the summer before admission ranged between 103,700 and 165,000 per cubic millimeter. A one-stage prothrombin time in August 1966 was 13.5 seconds (normal control 12.0 seconds). Prednisone administration, 50 milligrams daily, was instituted one month prior to hospital admission.

Upon admission to University Hospital, the patient complained only of excessive fatigue. Easy bruising, hematuria, melena and hematemesis were denied as was epistaxis. Physical examination revealed generalized lymphadenopathy and hepatosplenomegaly. No petechiae or ecchymoses were visible, a stool specimen was negative for occult blood and three urinalyses failed to demonstrate microscopic hematuria. A blood hemoglobin determination was 10.6 grams %, reticulocytes were 0.1% and the white blood cell count was 2000 cells per cubic millimeter (92% lymphocytes). The serum creatinine was 0.5 milligrams %, the total serum bilirubin was 0.8 milligrams % and the serum alkaline phosphatase was 1.9 Bodansky units. Platelets numbered 104,880 per cubic millimeter at the time of admission.

The patient received four units of whole blood without complications and corticosteroid therapy was continued. On the fifth hospital day, her temperature rose to 103° by rectum and four blood cultures were obtained (each of which subsequently yielded a pure culture of Enterobacter aerogenes). Intravenous tetracycline hydrochloride was administered. On the sixth hospital day, petechiae were first observed on the abdomen and blood platelets were found to number only 19,500 per cubic millimeter. Twenty-four hours later, petechiae and ecchymoses were described as "massive." The platelet count had fallen to 2000 per cubic millimeter but measurements of plasma fibrinogen content, one-stage prothrombin time and partial thromboplastin time were within normal limits. On the seventh hospital day, platelets numbered 1000 per cubic millimeter. Death occurred on the ninth hospital day.

Post mortem examination confirmed the diagnosis of lymphatic leukemia and demonstrated ecchymoses of the gastric mucosa, endocardium and renal pelves as well as a segmental infarction of the left lung.

Case 2: R. F., (Table 1 and Fig. 2.), a 51-year-old white male was admitted to University Hospital in June 1966 because of abdominal and back discomfort. The patient had resided at home since suffering a traumatic dislocation of the C_4-C_5 intervertebral joint in 1956.

Admission physical examination showed the patient to be a well-nourished white male quadriplegic with an indwelling urinary bladder catheter. The rectal temperature was 101°, respirations were 20 per minute, the pulse rate was 86 beats per minute. The blood pressure was 116/76 millimeters of mercury. The remainder of the physical examination was within

TABLE 1

COAGULATION STUDIES. PATIENT R. F.

	8th Day	*9th Day*	*10th Day*
Platelets (normal: 150,000-250,000/mm³)	31,000	36,000	27,600
Prothrombin Time (normal control: 12.0 seconds)	16 secs.	17 secs.	
Partial Thromboplastin Time (normal control: 38.0 seconds)	110 secs.		
Thromboplastin Generation Test	Prolonged*		
Plasma Factor V (% of normal)	30%		
Plasma Factors VII and X (% of normal)	30%		
Plasma Factor X (% of normal)	30%		
Plasma Prothrombin (% of normal)	20%		
Thrombin Time (normal control: 27.0 seconds)	91 secs.		
Thrombin-Time – Modified** (normal control: 27.0 seconds)	50 secs.		
Plasma Fibrinogen Concentration		330 mgs.%	263 mgs.%
Clot Retraction at 3 hours		absent	

*TGT consistent with Plasma Factor VIII deficiency.

**Modification of Thrombin Time procedure by combining equal parts of patient and control plasmas. Value consistent with presence of circulating antithrombin activity.

normal limits except for a firm 10 x 12 centimeter mass deep in the left upper quadrant.

The blood hemoglobin concentration was 7.0 grams % and the white blood cell count was 35,000 cells per cubic millimeter (84% PMN's, 15% band forms, 1% lymphocytes). A platelet count was not performed; however, the one-stage prothrombin time was 14.0 seconds (normal control 12.0 seconds). The serum creatinine was 3.3 milligrams %. Pyuria and albuminuria were present in the admission urine specimen. A chest x-ray was normal. Intravenous pyelography demonstrated a stag-horn calculus in the left kidney and numerous radio-opaque stones in the urinary bladder. A fresh urine specimen grew more than 10^6 colonies of Proteus mirabilis and Escherichia coli per milliliter of urine.

On the third hospital day, transurethral cystoscopy and bilateral percutaneous renal aspirations were performed. Six hours after the procedures shock occurred. Blood cultures were obtained (subsequently reported to be sterile) and cephalothin therapy, two grams intravenously every four hours, was begun. Levarterenol was employed to restore the systolic blood pressure to 100 millimeters of mercury. On the fourth hospital day, a left nephrolithotomy and nephrostomy were performed without anesthesia. Culture of a urine specimen obtained from the renal pelvis yielded a mixed growth of bacteria, (Escherichia coli, Proteus mirabilis and Streptococcus faecalis). Cephalothin therapy was continued but the patient required continuous vasopressor administration. Oliguria was present on the sixth hospital day. Urine specimens obtained from the urinary bladder and from the left renal pelvis on the seventh hospital day each yielded greater than 10^6 colonies of Pseudomonas aeruginosa per milliliter. The serum alkaline phosphatase measured 3.4 Bodansky units, the total serum bilirubin was 0.8 milligrams % and the serum creatinine was 2.3 milligrams %.

Upper gastrointestinal bleeding occurred on the morning of the eighth hospital day without evidence of bleeding elsewhere. The blood leucocyte count was 22,000 cells per cubic millimeter (63% PMN's, 31% band forms and 6% lymphocytes) and the hematocrit was 43%. Platelets were found to number only 31,000 per cubic millimeter and the results of blood coagulation studies (Table 1) were consistent with the existence of a consumptive coagulopathy. Cultures of renal pelvis and bladder urine specimens again yielded Pseudomonas aeruginosa and a single blood culture obtained 18 hours after the beginning of hematemesis subsequently yielded the same microorganism. Progressively increasing amounts of vasopressors were required to maintain the systolic blood pressure above 80 millimeters of mercury. Thrombocytopenia persisted. On the tenth hospital day, petechiae and ecchymoses were noted on the patient's chest and abdomen. Despite administration of fresh whole blood, the patient died on the eleventh hospital day.

Post mortem examination showed a 15.0 centimeter length of jejunum to be infarcted and the mesenteric arteriole supplying the infarcted segment to be occluded by a small thrombus. An abscess beneath the lesser omentum was connected by a fistula to a left perinephric collection of pus, a culture of which yielded Pseudomonas aeruginosa, Proteus mirabilis, Escherichia coli, and Streptococcus faecalis.

COMMENT

Both of the patients described in the present report experienced clotting disorders which could be reasonably ascribed to the initiation of intravascular coagulation by bacterial endotoxin. In both cases, a hemorrhagic diathesis appeared before death and in both episodes thrombosis was demonstrated at post mortem examination. In neither case, however, was histologic evidence of the generalized Shwartzman reaction described.

Consumptive coagulopathy has been amply described in reviews by Koller,[10] Verstraete et all[11] and Rodriguez-Erdmann[12] and its mechanism compared to that of the generalized Shwartzman reaction. Gram negative bacterial lipopolysaccharide effects release or activation of platelet factor 3.[13] This agent and plasma Factors XII, XI, IX, VIII, X and V constitute an intrinsic prothrombin-converting principle capable of producing sufficient

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Chicken Noodle	54	Cream of Mushroom	115
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Special note: Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision. Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Demulen is indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration, and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear, since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Demulen. Therefore, if such tests are abnormal in a patient taking Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Demulen may mask the onset of the climacteric. The pathologist should be advised of Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions; neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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thrombin to allow conversion of fibrinogen to fibrin.[10] Fibrinolysis of moderate proportions is believed to accompany intravascular coagulation[10] and may, on occasion, cause liberation of sufficient fibrinolytic split products to interfere with fibrin polymerization, thus further aggravating the hemorrhagic diathesis already extant.

The incidence of consumptive coagulopathy in patients with Gram negative bacillus septicemia is unknown; indeed, recent reviews of Gram negative bacteremia[14,15,16,17,18,19] have not noted this complication. The incidence of 2.6% reported herein is almost certainly too low, inasmuch as a third patient, not reported, demonstrated microinfarction of the pituitary gland following E. coli bacteremia and death at University Hospital during the period under study.

Summary

Two instances of consumptive coagulopathy occurred among 76 consecutive patients with Gram negative bacteremia at University Hospital, Boston, Massachusetts. The true incidence of intravascular coagulation in patients with Gram negative bacteremia is not known and will require prospective study for its proper definition.

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STATEMENT OF OWNERSHIP, MANAGEMENT AND CIRCULATION

(Act of October 23, 1962; Section 4369, Title 39, United States Code)

1. Date of filing: October 1, 1970.
2. Title of publication: The Journal of the Maine Medical Association.
3. Frequency of issue: Monthly.
4. Location of known office of publication: Bowdoin College Infirmary (P. O. Box 250), Brunswick, Maine 04011.
5. Location of the headquarters or general business offices of the publishers: Bowdoin College Infirmary (P. O. Box 250), Brunswick, Maine 04011.
6. Names and addresses of publisher, editor, and managing editor: Publisher: Maine Medical Association, P. O. Box 250, Brunswick, Maine 04011; Editor, Daniel F. Hanley, M.D., P. O. Box 250, Brunswick, Maine 04011; Managing Editor, None.
7. OWNER (If owned by a corporation, its name and address must be stated and also immediately thereunder the names and addresses of stockho'ders owning or holding 1 percent or more of total amount of stock. If not owned by a corporation, the names and addresses of the individual owners must be given. If owned by a partnership or other unincorporated firm, its name and address, as well as that of each individual must be given.) Maine Medical Association, P. O. Box 250, Brunswick, Maine 04011.
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2. Mail subscriptions	86	93
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I certify that the statements made by me above are correct and complete.

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The Use of Arterial or Venous Blood in Acid Base Balance

William H. Austin, M.D.*

For years, arterial blood has been considered a standard media for the measurement of pH, PCO_2 and HCO_3^-. The use of arterial as opposed to venous blood probably results from the anesthesiologist's and pulmonary physiologist's interest in the field plus the additional fact that venous blood is not an index of PO_2. Arterial PCO_2 is principally a function of ventilation whereas venous PCO_2 in addition is dependent on CO_2 production, patient activity, sample site, and to a small degree cardiac output.[1,2,3,4,5,6,7] The a-v PCO_2 difference most frequently used is 0 to 6 mm[8]; however, in several patients we studied with simultaneous a-v PCO_2 determination, the difference far extended these limits. As activity, alteration in cardiac output, CO_2 production and technical factors did not seem to be responsible for the changes, we sought to evaluate the role of alterations in ventilation as a cause for this discrepancy.

Although this paper does not establish the fact that ventilation changes account for the variations observed, it does indicate the magnitude of deviation in arterial PCO_2 which can occur as a result of increasing the minute volume.

Methods

Eight mongrel dogs weighing 8 to 16 Kg. were anesthetized with Nembutal® anesthestic, paralyzed with hexamethonium, intubated with a cuff endotracheal tube, and placed on a Harvard respirator. The PCO_2 values were allowed to stabilize for a period of 45 minutes at a 60 mmHg range. At that time, the ventilation was suddenly dropped by increasing the minute volume. The mean and range of PCO_2 values in both a & v samples are recorded in Fig. 1. The samples were drawn in heparinized glass syringes and the blood gas measurements were determined using an IL 313 Blood Gas Apparatus. Of note, is the fact that an indwelling needle placed in the femoral artery and an indwelling cannula in the saphenous vein were used for blood sampling. No mixed venous blood was used. After the control period, samples were taken at 30 second, one minute, two minute, five minute and ten minute intervals. Although not shown on the diagram, later samples were also taken.

Discussion

As noted, the a-v PCO_2 difference frequently sited in the physiological text is 0 to 6 mm and the pH from 0 to .04 with the venous pH being the lower. For the purposes of this study, we concentrated primarily on the PCO_2 since it showed the principle changes in question. Fig. 1

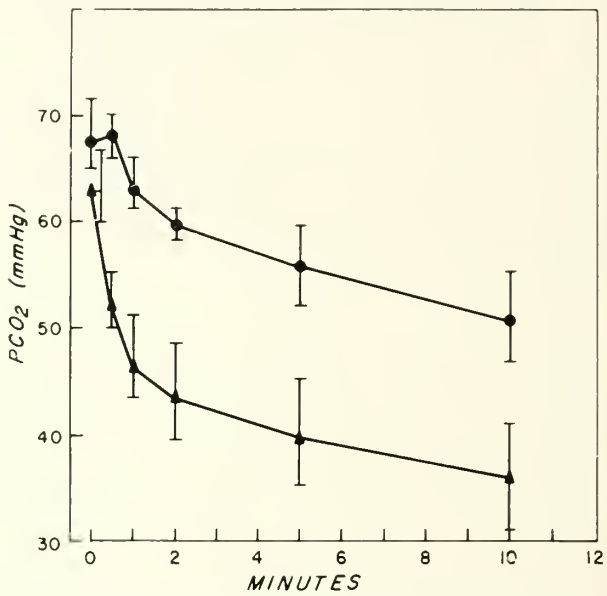

Fig. 1. The average and mean changes in venous (dot) and arterial (diamond) PCO_2 resulting from a two-fold increase in minute ventilation.

indicates that the a-v difference is at first narrow and that the arterial PCO_2 drops rapidly during the first few minutes of sampling. This is interpreted as hyperventilation which would be more likely to show up sooner in the arterial than in the venous sample. The latter is in contact with the CO_2 stores of the body. These data tend to indicate that the CO_2 stores become depleted during the procedure as a result of hyperventilation. By the time the first arterial sample is obtained, it appears that hyperventilation is reflected in the arterial samples as indicated by a 10 mm drop in PCO_2. The venous changes are much slower and therefore tend to reflect the steady state. The apparent hyperventilation that appears to persist is probably a depletion in the CO_2 stores.[9,10] The difficulty lies in the fact that it is difficult to assess the true significance of the arterial pH and PCO_2. If the sample is obtained rapidly, it is highly likely that the value represents a steady state; however, observation of the patient is not always a reliable index in hyperventilation, particularly since it can occur so rapidly and can produce such a dramatic change. For the patient on a ventilator, this is much less of a problem, particularly if the ventilation is controlled. It has been difficult to convince pulmonary physiologists in particular that arterial samples are not the sine qua non of acid base balance and that a venous sample represents merely a "reflection" of an arterial study. Some observors have sought to conclude that mixed venous blood would be an ideal material to assess.[3,4,5,6,7]

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Although it is true that venous blood is in contact with the CO_2 tissue stores and probably more accurately reflects the whole body acid base balance, there is a lack of consistency in mixed venous samples. From the published literature, there does not seem to be any good reason to prefer mixed venous blood over any other type of sample, particularly a sample drawn from the forearm. It is equally true that blood from the dorsum of the hand is probably no better than blood drawn from antecubital space. When blood for acid base studies is drawn from antecubital space, the tourniquet should be left in place and handpumping avoided.[11]

The practical aspect of evaluation of acid base balance is obvious from this discussion. Venous blood can usually be obtained with relative ease and probably more accurately reflects a steady state than the arterial samples. In evaluating the partial pressure of oxygen or oxygen tension, it is obvious that an arterial sample is mandatory.

Summary

For the routine evaluation of acid base balance, a venous sample from the antecubital vein is not only adequate but is probably superior to an arterial sample unless the PO_2 is desired. Certain exceptions have been noted. Mixed venous blood, since it is derived from the superior and inferior vena cava, is subject to a variety of factors which make it unsuitable for either routine or special studies. If one accepts the premise that acid base balance is important, its usefulness can be extended by measuring venous blood derived from the forearm. Despite good evidence in literature, it has been difficult to convince many physicians that venous blood is an adequate if not superior indicator of acid base balance.

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Maine Historical Society

The Membership Committee of the Maine Historical Society cordially invites members of the Maine Medical Association to join the Society on the occasion of the State's Sesquicentennial year.

As a member of the Society, you will be helping to collect, preserve and publish the history of our State, and maintain one of America's most notable historic houses, the Wadsworth-Longfellow House.

Members receive a quarterly **Newsletter** devoted to articles and bibliographies on Maine history and news of the Society, have access to the largest research Library on Maine history in the State, and are admitted free to the Wadsworth-Longfellow House.

Memberships are available in the following categories: Active $6.00, Sustaining $25.00, Life $200.00 from the Membership Chairman, Maine Historical Society, 485 Congress Street. Portland, Maine 04111.

Special Article

Paramedical Help in Maine Practice?*

LCDR Charles C. Morrison, MC, USN**

The Annual Scientific Meeting of the Maine Medical Association last June concerned itself in large part with innovation in medical practice. As may be expected with such a theme, the use of paramedical people in private practice was given prominent consideration. It is not that use of "non-M.D.s" is new to medical practice today; nurses, secretaries, receptionists and administrators have long been present. The concept that is presented as new is that a "medical" assistant may be used directly in patient care to perform some aspects of the physical exam or absorb the "routine" which presently consumes a physician's time.

In those clinics where such persons have become active members of the medical team, the involved physicians have found their time and knowledge applied more effectively, their medical care more complete, and their professional satisfaction greatly enhanced.

The military has long utilized the "corpsman" to perform tasks in this manner. Each year, many persons trained in basic first aid, physical exam procedures, laboratory work, x-ray procedures and electrocardiograph methods are released from active duty only to become lost to the medical work force.

Why are the talents of these medically trained persons not put to use by private civilian practices? Of course, some persons are simply not interested in further work in the medical field; others pursue a different level such as attending medical school. Two additional reasons appear considerably more significant.

1. The physician is not aware of how a paramedical person can be used efficiently – and safely – in his practice. Actually, any procedure which is *repeatedly* performed in the daily routine of a physician can probably be *learned* by a paramedical person. The efficient use of a "physician's aid" requires that a doctor stand back and look at those procedures which he repeats in this manner, decides what can be clearly defined, and delegates the responsibility to persons with the ability to perform the steps he has outlined.

Legally, or perhaps morally, most physicians would not presently permit a procedure to be performed on their patient which he has not defined himself or that will be done by persons whose competence he holds in doubt. The guidelines a physician may use in adopting paramedical personnel to his practice are little different from those he now includes as standard for his own guidance.

2. The military corpsman is trained to treat military personnel. Although he possesses a great deal of "first line" medical information, the difference between application to active duty personnel is great – and previously insurmountable. The necessary public relations professionalism is not a concept taught military corpsmen.

The Naval Air Station, Brunswick, has set up a family clinic paramedical training program. The purposes of the program are to add this concept of personality consideration to a corpsman's approach, as well as to teach the potential physician's assistant to function at a level both helpful to the physician and satisfying to himself.

The program will be presented to interested corpsmen at three levels:

1. Initially, he is required to review basic anatomy, psychology and medical principles. This phase acts as a motivational screen for many.

2. In the second phase, the corpsman screens patients under rigidly prescribed criteria under direct physician supervision. At this point, a judgment is made as to the corpsman's suitability for direct patient contact.

3. The last phase of his training is under the supervision of a previously trained physician's aid. At this time, he further reviews the defined limits under which he is expected to work, and perfects his abilities within the prescribed framework. At this point, he must be completely familiar with patient screening forms and methods.

As the training program is being carried on at a time when the Dispensary is adopting the "Problem-Oriented Record System," the paramedic will be versed in this concept of record keeping and the automated data gathering systems which are a part of it.

Although the program is aimed at providing additional medical training to military personnel, the possibility exists that the Dispensary may serve as a "con-

*"The opinions or assertions contained herein are the private ones of the author and are not to be considered as official nor as reflecting the views of the Bureau of Medicine and Surgery of the Navy Department or the Naval Service at large."

**Programmed Patient Care Clinic, NAS Dispensary, Brunswick, Maine 04011.

tact point" for referral of interested and trained corpsmen to physicians who might find their talents of value in their private practice. If it were possible to support the present training program with an expressed demand from Maine physicians, the program could well be enlarged to provide a regular source of family clinic trained corpsmen to Maine practices.

If a physician's aid would be of value to your practice, or if you would desire an outline of our training syllabus, an expression of such interest should be directed to:

LCDR Charles C. Morrison, MC, USN
Programmed Patient Care Clinic
NAS Dispensary
Brunswick, Maine 04011

Services for the Mentally Retarded Evaluation Clinic

WILLIS M. GOWEN, M.D.*

In the spring of 1967, a program to evaluate and make recommendations for any mentally retarded resident in the State of Maine was established by Dr. Peter W. Bowman, Director of the Pineland Hospital and Training Center.

This program at Pineland Hospital and Training Center includes the services of: Physicians, Social Workers, Psychologists, Psychiatrists, Teachers in Special Education, Speech and Hearing Specialists, Physical Therapists and Occupational Therapists. When needed, members of the Consulting Staff in Neurology, Orthopedics, Vocational Training, Physical Medicine, Genetics and other fields are available.

All patients who go through this Clinic receive a thorough and comprehensive investigation. It normally takes about six hours for a patient to complete such an examination.

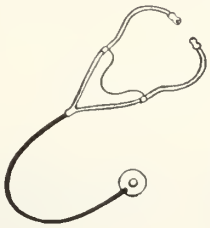
After all information and laboratory data are completed, the team, as a whole, meets in conference. Each member of the evaluation team discusses the aspects of the case as it is concerned in his particular area. After all departments are heard, evaluations and recommendations are made.

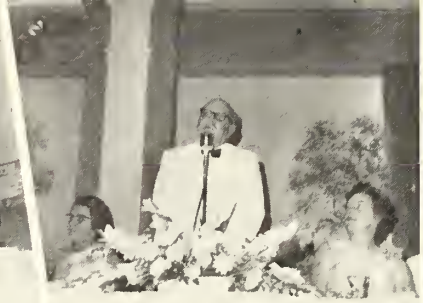
The team advises institutionalization only after it has explored all the community resources available to the particular patient. If community facilities are available and are more appropriate for the patient, then the team helps the family to avail themselves of these community resources. A report is written and will be forwarded to the referring physician upon his request.

This service is available to all mentally retarded or "slow-learners" of our State, regardless of financial status. Referral may be made to the Director by the physician, family, school, community health services, mental health services, social agencies or any other professional in the community. Such referrals and inquiries are welcome.

Pineland Hospital and Training Center has just ended the third year of this program and 400 individuals have been evaluated. This Evaluation Program is another step in broadening services for the mentally retarded.

*Director, Evaluation Clinic, Pineland Hospital and Training Center, Pownal, Maine 04069.





THANKS FOR A RARE PRIVILEGE

To Members of the Maine Medical Association:

There are times when words are not adequate to express one's feelings and this is one of those times — because "thank you" cannot begin to tell you all how much I appreciate the honors extended to me at the annual banquet of the Association in June. The "purse" presented by Dr. Branch, the gold pin by Dr. Stitham, the Honorary Membership announced by Dr. Glassmire, and, the subject of the program being "me" were indeed a surprise (that I still get 'prickles' over) and something that I shall never forget. As a matter of fact I was so surprised and overwhelmed that I was unable to express myself at that time and hence this expression of my appreciation; appreciation not only for these honors but for the rare privilege of having been a part of this Association for these many years and to have so many pleasant memories to carry with me into retirement.

I understand that Dr. Branch and Dr. Hanley originated and carried through this program and managed to keep me in the dark, even ignoring all my requests for a "subject" for the speaker for the annual banquet who was Dr. Branch — a very special thanks to them.

E.M.K.

THE PICTURES

E.M.K. honored at 1970 annual banquet by announcement of Honorary Membership by Dr. Glassmire, President-elect, presentation of "purse" by Dr. Branch, President, and gold pin by Dr. Stitham, Council Chairman. Here she presents the Association's Honorary Pins to Drs. Woodcock, MacDougall, Thaxter, Kinghorn and Russell, and receives one of several standing ovations. The bottom row also shows the "Officers" in their new roles, Dr. Stitham, President-elect, Dr. Glassmire, President and Dr. Branch, retiring President, and E.M.K. taking it easy as her successor, Patricia Bergeron, takes over.

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

Reflections on the Use of Propranolol in Angina Pectoris

Medical and surgical efforts in the treatment of angina pectoris . . . have been mainly directed toward attempts at increasing myocardial blood supply. . . . we have seen the introduction and widespread use of a large number of . . . nitrate preparations, . . . (and) our surgical colleagues have devised ingenious methods to promote myocardial revascularization from extracardiac sources. In both instances, their beneficial effects remain the subject of debate and controversy. . . .

The recent development of drugs capable of selectively blocking beta-sympathetic receptor sites has provided us with a new approach to the treatment of angina pectoris. . . . The vast majority of published reports indicate that in well-controlled, short-term clinical trials, propranolol, when given in adequate doses, is effective in reducing the frequency and severity of anginal attacks and improves exercise tolerance. Indeed, preliminary reports also suggest that in patients with very advanced coronary artery disease and severe angina, propranolol may influence the natural history of this disease. . . . Wolfson et al have reported data suggesting that the incidence of sudden death and acute myocardial infarction seems to be reduced, compared to similar groups receiving more traditional therapy or subjected to internal mammary artery implants. . . .

The exact mechanism whereby propranolol is effective in angina is uncertain. Its administration is followed by many important hemodynamic changes, resulting both in an increase or a decrease in myocardial oxygen requirements. . . . In most cases, the net effect is a reduction in myocardial oxygen consumption. . . . Thus, by blocking myocardial beta-adrenergic receptors, propranolol appears to attenuate or prevent the increase in myocardial oxygen requirements resulting from the sympathetic stimulation taking place during exercise or emotional stress.

. . . Propranolol's quinidine-like action has been stressed. It's anti-arrhythmic properties may be of some benefit to patients whose anginal attacks are associated with paroxysmal arrhythmias.

. . . As its use becomes more widespread, several important considerations must be stressed in assessing its merits in the treatment of angina pectoris. These considerations pertain to the variability in dosage . . ., to potential hazards related to its use, and to adverse effects. It is evident that some patients . . . do not benefit from propranolol.

. . . It is also important to recognize that although the average effective daily dose is of the order of 250 mgs., it may vary from 60 to 400 mgs. . . . Thus, controlled clinical trials on a fixed dose may be difficult to evaluate and may, indeed, underestimate the properties of the drug.

Beta-adrenergic blockage may, theoretically, induce bronchospasm. . . . Since propranolol increases atrioventricular conduction time and, by blocking adrenergic receptors, has a pronounced negative chronotropic effect, it is also contraindicated in patients with pre-existing sinus bradycardia or atrioventricular block.

The most serious hazard . . . is related to its negative inotropic effect. The sick heart depends on sympathetic tone, and beta-adrenergic blockade may precipitate overt congestive heart failure in patients with borderline compensation. . . . Since the positive inotropic effect of digitalis is not reversed by the beta-adrenergic blockade, we prefer to administer digitalis prior to giving propranolol.

. . . In centers where propranolol is used for angina pectoris, familiarity with the pharmacologic properties of glucagon should be acquired, so that it can be used, if necessary, in patients developing cardiogenic shock while receiving beta-adrenergic blocking agents.

Adverse reactions to propranolol have been generally mild and well tolerated, and rarely necessitated its discontinuation. Nausea, abdominal cramps, loose bowel movements, and occasionally diarrhea have been encountered. These are usually transient and become less troublesome after 3 to 6 weeks of treatment. . . . several of our subjects complained of a mild fatigue or lack of energy. . . . In subjects with severe and frequent angina, however, this adverse effect seems eclipsed by the noticeable decrease in anginal symptoms.

Propranolol is a potent drug, offering an interesting new concept in the treatment of angina pectoris. Its beneficial effects in the short-term treatment of angina are well established and some evidence suggests that it may improve prognosis. . . . There are distinct contraindications to its use, and definite precautions to be followed. . . . Although the potential hazards . . . must be stressed, when used properly it is a very effective agent and its results have been gratifying. Its place in the long-term treatment of coronary artery disease is promising, and awaits further experience.

Submitted by Jacob B. Dana, M.D., Maine Heart Association.

Reference: Mizgala, Henry F., et al, American Heart Journal, Vol. 80, pages 428-430, 1970.

AMERICAN CANCER SOCIETY - MAINE DIVISION, INC.

Brunswick, Maine

Uterine Cancer

"Now's the time to sharply reduce the estimated 13,000 yearly deaths from uterine cancer," declared Paul S. Hill, Jr., M.D., President of the American Cancer Society, Maine Division, Inc.

Dr. Hill said, "It's up to you, and you, and you to use and influence the use of the simple and painless Pap test for the early detection of cancer throughout the State of Maine.

"The death rate from cancer of the uterine cervix has declined more than half in the last 30 years largely because of the Pap test, which can spot the disease before symptoms appear.

"Based on the microscopic examination of cast-off cells, the test is quick and painless, and is named after Dr. George N. Papanicolaou.

"A recent Gallup poll showed a sizable increase in American women's familiarity with the Pap test — up from 50 percent in 1961 to 90 percent in 1970. But where 48 percent said they'd had it in 1963, only 53 percent said they'd had it in 1970 — a slight percentage increase which indicates a lack of action by those who knew it.

"Women need not die of uterine cancer. That's the vital message the American Cancer Society wants everyone to know. It's the theme of our latest film, 'It's Up to You.' But I'll go a step further and urge fathers and husbands to say to their loved one — 'It's Up to You — to get your Pap test!'

"The film tells the story of one woman as she attends a public lecture on uterine cancer by a doctor in her community. She had been putting off having a Pap test, but is spurred to action by the doctor's talk. Later, after she's had the test, she is relieved to know it was negative. She resolves to have a Pap test regularly.

"Think of yourself as your doctor's partner in good health," Dr. Hill said. "He can help you if you visit him regularly whether or not there's something wrong. But also learn all of cancer's Seven Warning Signals and see him if you have one.

"Then educate a friend who might be hesitating to have a checkup."

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When girth gets out of control, TEPANIL can provide sound support for the weight control program you recommend. TEPANIL reduces the appetite—patients enjoy food but eat less. Weight loss is significant—gradual—yet there is a relatively low incidence of CNS stimulation.

Contraindications: Concurrently with MAO inhibitors, in patients hypersensitive to this drug; in emotionally unstable patients susceptible to drug abuse.

Warning: Although generally safer than the amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, unpleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptics an increase in convulsive episodes has been reported. Sympathomimetic cardiovascular effects reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others. Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema. Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. Specific reports on the hematopoietic system include two each of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Convenience of two dosage forms: TEPANIL Ten-tab tablets: One 75 mg. tablet daily, swallowed whole, in midmorning (10 a.m.); TEPANIL: One 25 mg. tablet three times daily, one hour before meals. If desired, an additional tablet may be given in midevening to overcome night hunger. Use in children under 12 years of age is not recommended.

T-006A / 1/70 / U S PATENT NO. 3,001,910

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

Painful night leg cramps...

unwelcome bedfellow for any patient– including those with arthritis, diabetes or PVD

One thing patients can sleep without, particularly patients with chronic disease conditions such as arthritis, diabetes or PVD, is painful night leg cramps. Although seldom the presenting complaint, night leg cramps can tie your patients up in painful knots. Now, just one tablet of QUINAMM at bedtime can usually bring an end to shattered sleep and needless suffering. Your patients will sleep restfully—gratefully—with QUINAMM, specific therapy to prevent painful night leg cramps.

Prescribing Information—Composition: Each white, beveled, compressed tablet contains: Quinine sulfate, 260 mg., Aminophylline, 195 mg. **Indications:** For the prevention and treatment of nocturnal and recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis and static foot deformities. **Contraindications:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions/Adverse Reactions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets.

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON-MERRELL INC.
PHILADELPHIA, PENNSYLVANIA 19144

Quinamm™ Specific therapy for night leg cramps
(quinine sulfate 260 mg., aminophylline 195 mg.)

Q915A 1/79

Necrologies

Francois J. Faucher, M.D.

1893-1970

Dr. Francois J. Faucher, 77, of Grand Isle, Maine died on September 12 at a Fort Kent hospital following a short illness.

He was born in St. Euphreme, Quebec on April 28, 1893, son of Francois and Virginie P. Faucher.

Dr. Faucher received his medical degree from the University of Montreal Faculty of Medicine in 1919. He located in Grand Isle in 1919 and practiced there until the time of his death.

He was an honorary member of the Aroostook County Medical Society and the Maine Medical Association, having received a 50-year pin in 1969. Dr. Faucher was also a member of the American Medical Association, had served as President of the Aroostook County Medical Society and was medical examiner for over twenty years.

Surviving are four sons, Conrad and John of Grand Isle, the Rev. Arthur Faucher of Montreal, Quebec and Clarence of South Weymouth, Massachusetts; two daughters, Mrs. Carmel Olden of South Weymouth, Massachusetts and Mrs. Rollande Dionne of Madawaska; two sisters, Mrs. Denise Qurion of St. Pierre, Broughton, Quebec and Sister Marie of the Sacred Heart, Quebec.

Robert A. Bearor, M.D.

1922-1970

Dr. Robert A. Bearor, 48, of Portland, Maine, associate radiologist at the Maine Medical Center since 1962, died on September 25 following a long illness.

He was born in Madison, Maine on January 12, 1922, son of Eugene P. and Mary S. Bearor.

Dr. Bearor was graduated from the University of Wisconsin in 1944 and received his medical degree from Boston University School of Medicine in 1948. He interned at the Central Maine General Hospital from 1948 to 1949 and served a residency in internal medicine at the Pratt Diagnostic Clinic in Boston in 1950.

Dr. Bearor served in the U.S. Army Medical Corps as Group Surgeon with the 32nd Army Engineers from 1951 to 1953. From 1953 to 1955, he completed a medical residency at the Veterans Administration Hospital in Memphis, Tennessee and then located in Madison, Maine in 1955 for two years. He served a residency in radiology from 1957 to 1960 at the Beckley Memorial Hospital in West Virginia and completed his radiological studies at the University of Pennsylvania in 1962. Dr. Bearor was then appointed an associate in the Department of Radiology at the Maine Medical Center.

He was a member of the Cumberland County Medical Society, the Maine Medical Association and the American Medical Association. Dr. Bearor was also certified by the American Board of Radiology in Diagnostic Radiology, Therapeutic Radiology and Nuclear Medicine, a member of the New England Cancer Society, president of the Maine Radiological Society, a member of the Radiological Society of North America, the New England Roentgen Ray Society, the Society of Nuclear Medicine and was an instructor at the Maine Medical Center School of Radiologic Technology.

Surviving are his widow, Mary Lyons Bearor; two sons, Peter and Gregory; one daughter, Susan, all of Portland; his mother, Mrs. Eugene Bearor of Madison; a sister, Mrs. B. G. Farris of San Diego, California; and two brothers, Rene Bearor of Madison and Lionel Bearor of Trangle, Virginia.

Ec-
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omy!

Dicarbosil®
ANTACID

Your ulcer patients and others will appreciate it. Specify DICARBOSIL 144's—144 tablets in 12 rolls.

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Menrium® treats the menopausal symptoms that bother him most.

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Division of Hoffmann-La Roche Inc
Nutley, New Jersey 07110

His wife has a lot of different
nenopausal symptoms, but only a few
eally irritate *him*. Her hot flashes, her
ertigo, her palpitations—that's *her*
roblem. What really bothers him is
er nervousness, her irritability and
er excessive anxiety, often expressed
y endless "book-shuffling, chain-
moking, reading-lamp" insomnia!

Menrium takes care of hot flashes,
ertigo, palpitations in most
nenopausal women. Menrium
rovides the well-known antianxiety
ction of chlordiazepoxide (Librium®)
nd water-soluble esterified estrogens.
t therefore relieves more symptoms
han either component separately.
t takes care of the vasomotor
ymptoms as well as the emotional
ymptoms. This means the symptoms
hat bother his wife most. And the
ymptoms that irritate him most.

So, to help them both get through
er menopause, remember Menrium.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Management of manifestations generally associated with the menopausal syndrome—anxiety and tension, vasomotor complaints and hormonal deficiency states.

Contraindications: Women with cancer of breast or genitalia, except inoperable cases, and those with known hypersensitivity to chlordiazepoxide and/or esterified estrogens.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Exclude other possible causes of menopausal syndrome manifestations, such as pregnancy. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) similar to those seen with barbiturates have been reported following discontinuance of chlordiazepoxide HCl. Potential benefits of use in pregnancy, lactation or women of childbearing age should be weighed against possible hazards to mother and child. Clinical data inadequate on safety in pregnancy.

Precautions: In elderly and debilitated patients, limit dosage to smallest effective amount of chlordiazepoxide (initially 10 mg or less per day) to preclude ataxia or oversedation; increase gradually as needed and tolerated. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects—particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in patients with impaired renal or hepatic function. Paradoxical reactions to chlordiazepoxide (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in the treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation very rarely reported in patients receiving Librium® (chlordiazepoxide) and oral anticoagulants.

Adverse Reactions: Untoward effects seen with either compound alone may occur with Menrium. With chlordiazepoxide, drowsiness, ataxia and confusion reported in some patients, particularly in the elderly and debilitated; while usually avoided by proper dosage adjustment, these are occasionally observed at lower dosage ranges. Also reported have been a few instances of syncope; isolated occurrences of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido, and occasional reports of blood dyscrasias, including agranulocytosis, jaundice and hepatic dysfunction. Periodic blood counts and liver function tests advisable during protracted treatment. Changes in EEG patterns (low-voltage fast activity) observed during and after chlordiazepoxide treatment.

With estrogens, headache, nausea and vomiting, anorexia, gastrointestinal discomfort, dysuria and urinary frequency, jitteriness, breast engorgement, formation of breast cysts, skin rashes and pruritus occasionally seen. Administration may also be associated with uterine bleeding and/or followed by withdrawal bleeding.

Usual Dosage: One tablet t.i.d. for 21 days, followed by one-week rest periods.

Menrium® T.I.D.

5 mg chlordiazepoxide	5-2	0.2 mg water-soluble esterified estrogens
5 mg chlordiazepoxide	5-4	0.4 mg water-soluble esterified estrogens
10 mg chlordiazepoxide	10-4	0.4 mg water-soluble esterified estrogens

This contract provides physicians' services and benefits to the extent herein defined and limited.

Blue Shield Plans

OF THE

Associated Hospital Service of Maine

(Herein Called A H S)

PORTLAND, MAINE

Certificate of Coverage for Physicians' Service Benefits

This is to Certify: That the Subscriber and Family Members, if any, named on the Subscriber's Identification Card issued as a part of this Contract, are entitled to benefits in accordance with the terms, conditions and provisions appearing hereinafter and made a part hereof.

In Witness Whereof Associated Hospital Service of Maine (a Non-profit Maine Corporation) has duly executed this Contract.

Countersigned by:

President

Chairman of the Board

PHY[illegible] any Member who is [illegible]lly defined in Article

Article I [illegible]finiti[illegible] Member who does

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What Makes Blue Shield Different?

1. Our unique relationship with the medical profession. The Health Insurance Committee of the Maine Medical Association is the official policy-making body of the Maine Blue Shield Plan. Each county society is represented on that Committee; each specialty group is represented on the Advisory Committee. And seven physicians nominated by the Maine Medical Association sit on Blue Shield's Board of Directors.
2. Blue Shield is non-profit, community-oriented.
3. We could go on — direct payment to doctors, our new "usual and customary" coverage, professional relations representative available to visit doctors' offices, etc., etc. — but we think you know that Blue Shield is a little more than "just another insurance company."

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TO RECOVERY

Orenzyme® Bitabs

Trypsin: 100,000 N.F. Units, Chymotrypsin: 8,000 N.F. Units; equivalent in tryptic activity to 40 mg. of N.F. trypsin

The causes of vaginitis are multiple

Trichomonads . . . monilia . . . bacteria
You can depend on AVC—comprehensive therapy that combats all three major vaginal pathogens, alone or in combination.

AVC
Cream (aminacrine hydrochloride 0.2%, sulfanilamide 15.0%, allantoin 2.0%)

Suppositories (aminacrine hydrachloride 0.014 Gm., sulfanilamide 1.05 Gm., allantoin 0.14 Gm.)

Contraindications: Known sensitivity to sulfonomides.
Precoutions/Adverse Reoctions: The usual precautions for topical ond systemic sulfonamides should be observed becouse of the possibility af absarptian. Burning, increased local discamfart, skin rash, urticaria or other monifestations of sulfonomide toxicity ore reasons to discontinue treatment.
Dosoge: One applicotarful or ane suppository intravaginally once or twice daily.
Supplied: Cream – Four-ounce tube with or withaut applicatar. Suppositories – Box of 12 with applicatar.

TRADEMARK: AVÇ AV-007A 7/70 Y-149

THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON MERRELL INC
PHILADELPHIA, PENNSYLVANIA 19144

AVC
The treatment is singular

Drip stopped, Congestion cleared

For upper respiratory allergies and infections, up to 12 hours clear breathing on one tablet. Dimetapp Extentabs® do an outstanding job of helping clear up the stuffiness, drip and congestion of colds and upper respiratory allergies and infections. Each Extentab keeps working up to 12 hours. And for most patients drowsiness or overstimulation is unlikely.

INDICATIONS: Dimetapp is indicated for symptomatic relief of the allergic manifestations of respiratory illnesses, such as the common cold and bronchial asthma, seasonal allergies, rhinitis, conjunctivitis, and otitis. CONTRAINDICATIONS: Hypersensitivity to antihistamines. Not recommended for use during pregnancy. PRECAUTIONS: Until patient's response has been determined, he should be cautioned against engaging in operations requiring alertness. Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. SIDE EFFECTS: Hypersensitivity reactions including skin rashes, urticaria, hypotension and thrombocytopenia, have been reported on rare occasions. Drowsiness, lassitude, nausea, giddiness, dryness of the mouth, mydriasis, increased irritability or excitement may be encountered. DOSAGE: 1 Extentab morning and evening. SUPPLIED: Bottles of 100 and 500.

A·H·ROBINS
A. H. Robins Company
Richmond, Va 23220

Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg.; phenylephrine HCl, 15 mg.; phenylpropanolamine HCl, 15 mg

when an unnerving experience compounds the pain

the compound analgesic that calms instead of caffeinates

In addition to pain, this patient has experienced anxiety, fear, embarrassment, and frustration. No doubt these psychic factors actually increased her perception of pain. Surely the last thing she needs is an analgesic containing caffeine. The logical choice is Phenaphen with Codeine. It provides a quarter grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can control the pain more effectively. It's no accident that the Phenaphen formulations contain a sedative rather than a stimulant. Don't you agree, Doctor, that psychic overlay is an important factor in most of the accident cases you see?

Phenaphen®

with Codeine

Phenaphen with Codeine Nos. 2, 3, or 4 contains: Phenobarbital (¼ gr.), 16.2 mg. (warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Hyoscyamine sulfate, 0.031 mg.; Codeine phosphate, ¼ gr. (No. 2), ½ gr. (No. 3), or 1 gr. (No. 4) (warning: may be habit forming). **Indications:** Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.
A. H. Robins Company, Richmond, Va.

A·H·ROBINS

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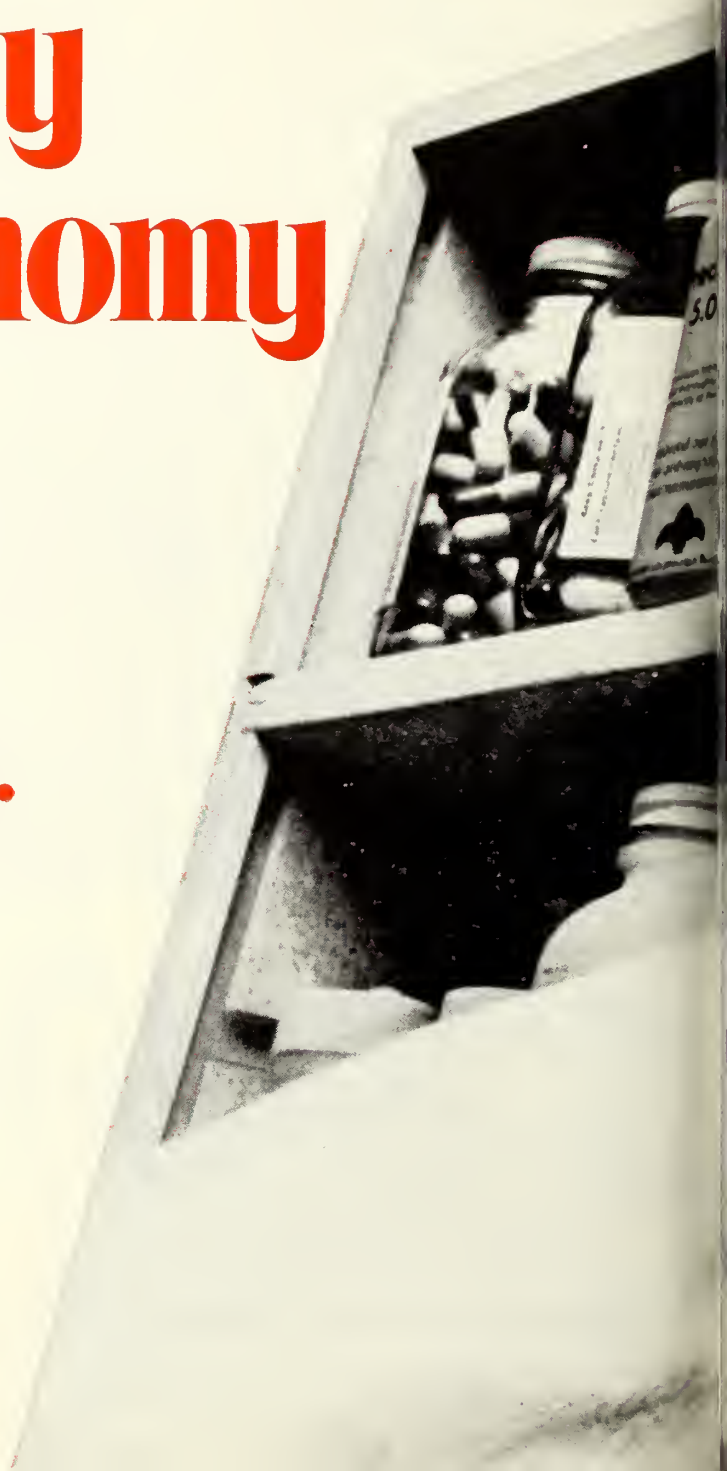
Guide his hand to quality and economy



Specify Deltasone® 5 mg.
(prednisone, Upjohn)

an economical
prednisone
that's made
a name for itself

Upjohn The Upjohn Company, Kalamazoo, Michigan 49001

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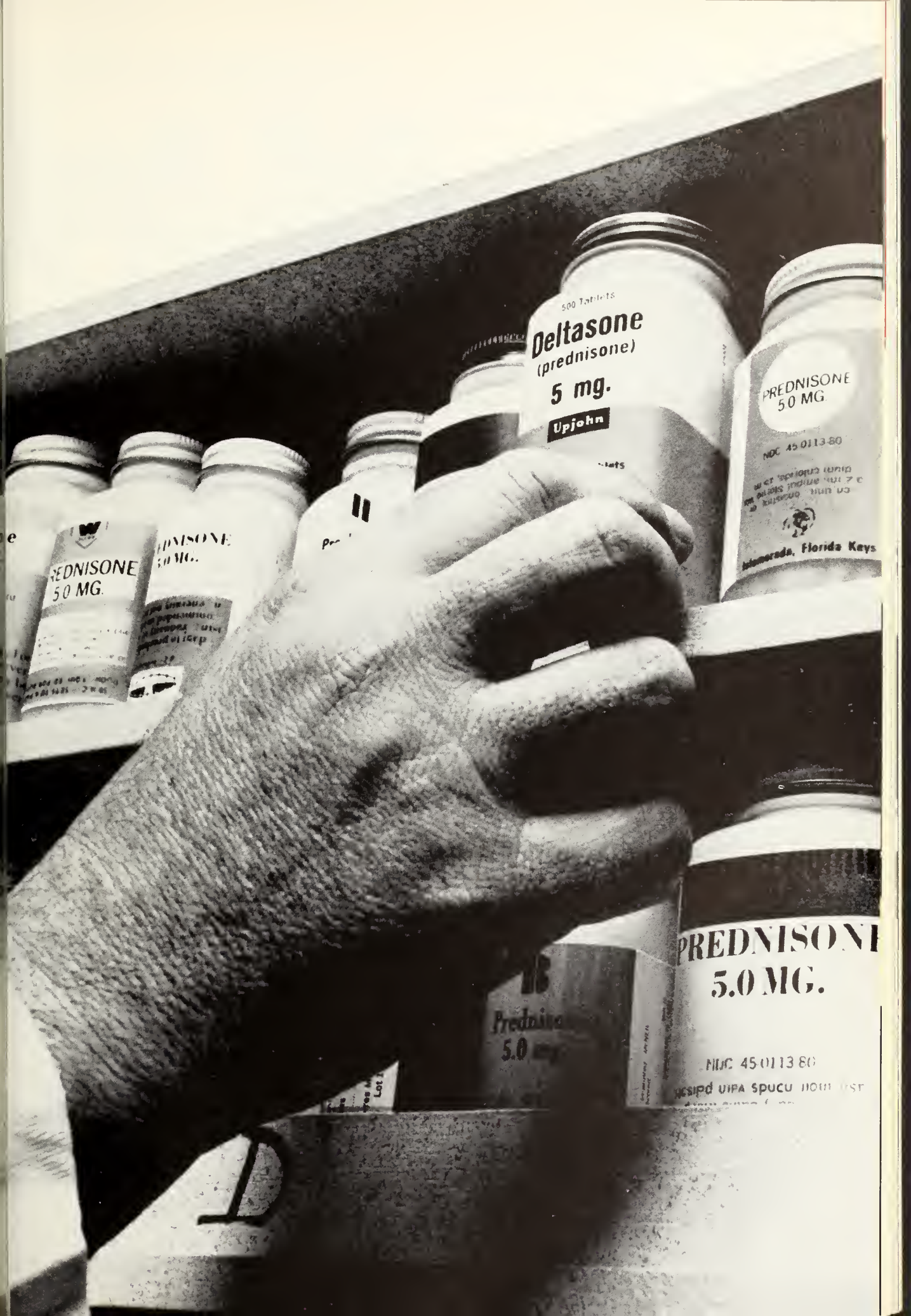
500 Tablets
Deltasone
(prednisone)
5 mg.
Upjohn
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5.0 MG.
NDC 45-0113-80
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PREDNISONE
5.0 MG.
PREDNISONE
5.0 MG.
NDC 45-0113-80

DELTASONE® TABLETS—2.5 & 5 mg.
(prednisone, Upjohn)

The potency of prednisone exceeds cortisone in glucocorticoid and anti-inflammatory activity by about five times on a weight basis, but is considerably less active than cortisone in mineralocorticoid activity.

Indications are the same as those for other anti-inflammatory steroids. Representative uses include collagen diseases, allergic diseases, generalized dermatoses, acute ocular inflammatory disease, certain lymphatic neoplastic diseases, ulcerative colitis and nephrosis. *Important:* Prednisone, like cortisone, is a potent therapeutic agent influencing the biochemical behavior of most, if not all, tissues of the body. Because it manifests little sodium-retaining activity, the usual early sign of cortisone overdosage (i.e., increase in body weight due to fluid retention) is not a reliable index. Hence, recommended dose levels should not be exceeded, and all patients should be under close medical supervision. All precautions pertinent to the use of cortisone apply to Deltasone (prednisone).

Contraindications: As for all other corticoids. *Considered Absolute*—herpes simplex keratitis, acute psychoses and latent, healed or active tuberculosis. May be lifesaving in certain cases of pulmonary or meningeal tuberculosis, but should be used only in conjunction with adequate and effective antituberculous therapy to which causative organisms are shown to be sensitive. *Considered Relative*—active or latent peptic ulcer, Cushing's syndrome, diverticulitis, fresh intestinal anastomoses, osteoporosis, renal insufficiency, thromboembolic tendencies, psychotic tendencies, diabetes mellitus, hypertension, local or systemic infections including vaccinia, varicella and other exanthematous diseases, and fungal infections, and, pregnancy particularly during the first trimester because of observation of fetal anomalies in experimental animals. If necessary to give corticosteroids during pregnancy, watch newborn infants closely for signs of hypoadrenalism and institute appropriate therapy if signs appear.

If corticoids are used in the above conditions, weigh risks against benefits.

Precautions: Deltasone should be given only with full knowledge of characteristic activity of and varied responses to corticoids. Because of inhibiting effect on fibroplasia, corticoids may mask signs of and enhance spread of infection; hence, watch patients closely, and if intercurrent infection occurs, control with appropriate antibacterial measures. If possible, avoid abrupt cessation of corticosteroid therapy because of the danger of superimposing adrenocorticoid insufficiency on the infectious process. Prolonged hormone therapy usually causes a reduction in the activity and size of the adrenal cortex. When discontinuing therapy, relative adrenocortical insufficiency may be avoided by gradual reduction of dose. However, a potentially critical degree of insufficiency may persist asymptomatically for some time even after gradual discontinuation of adrenocortical steroids. Therefore, if a patient is subjected to significant stress, such as surgery, trauma, or severe illness while being treated, or within one year (occasionally up to two years) after treatment has been terminated, hormone therapy should be augmented or reinstituted and continued for the duration of the stress and immediately following it. Since mineralocorticoid secretion may be impaired, salt and/or desoxycorticosterone should be administered conjunctively. It is preferable to use a soluble hormone preparation in the immediate preoperative and postoperative periods.

Although unlikely with Deltasone, average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary. Glucocorticoid steroids may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestations of latent diabetes mellitus may be precipitated. Corticosteroids may aggravate myasthenic symptoms in myasthenia gravis and should be given with proper precautions.

Muscle weakness, in some instances, attributed to hypopotassemia, has been reported following prolonged systemically administered corticoids. Excessive potassium loss, like excessive sodium retention, is not likely to be induced with effective maintenance doses of Deltasone (prednisone), however, keep this e in mind and perform periodic serum potassium determinatior patients on prolonged corticoid therapy. Muscle weakness oc ring with normal serum potassium levels may be due to disturba in muscle metabolism. Severe myopathy is associated with stantial doses of steroids for prolonged periods, and evide indicates it occurs more frequently with 9-alpha-fluro steroids. placement with non-fluorinated steroid has, in some instances sulted in improvement.

Retardation of linear growth, roughly proportional to dose, been noted in children on corticoids for six months or more. Foll ing cessation of therapy, growth rate may be accelerated. Th fore, carefully observe growth of children on prolonged corti and if growth is retarded, reduce dose sufficiently to permit reco before epiphyseal closure. Make every effort to avoid cortic during pregnancy, since spontaneous remission of some disea such as rheumatoid arthritis may occur. Long term corticoid ther may evoke hyperacidity or peptic ulcer, therefore, as prophyla an ulcer regimen and antacid are highly recommended. Take X-r in peptic ulcer patients complaining of gastric distress, a whether or not changes are noted, an ulcer regimen is rec mended. Since prednisone causes less salt and water reten than many other glucocorticoids, patients should be obser closely for development of undesirable hormonal effects that less obvious indications of steroid toxicity than edema and hyp tension due to salt and water retention. Continued supervisior patients after cessation of therapy is essential, since there may a sudden reappearance of severe disease manifestation.

Adverse Reactions: Adverse reactions associated with use of cc coids include: Cushing's syndrome, moon facies, supraclavic fat pads, hirsutism, striae and acne; relative adrenocortical insu ciency particularly in time of stress due to trauma, surgery severe illness; protein catabolism with negative nitrogen balan electrolyte imbalance; alteration of glucose metabolism with agg vation of diabetes mellitus including hyperglycemia and glycosu osteoporosis reversible only with difficulty; spontaneous fractur aseptic necrosis of the hip and humerus; activation and compli tion of peptic ulcer including perforation and hemorrhage; agg vation or masking of infection; increased blood pressu convulsions; petechiae and purpura; menstrual irregularities cluding amenorrhea, spotting or prolonged bleeding; insomr psychic disturbances especially abnormal euphoria; nervousne posterior subcapsular cataracts occasionally requiring extracti increased intraocular tension; increased intracranial pressure w papilledema (pseudotumor cerebri); pancreatitis; necrotizing an itis; thinning of scalp hair; suppression of growth in childr thromboembolic complications; facial erythema; allergic skin rea tions; ulcerative esophagitis; sweating; vertigo; weakness; myc athy; headache; exophthalmos. Adverse reactions are usua reversible and usually disappear when drug is discontinued.

Supplied: 2.5 mg., scored—bottles of 100 tablets. 5 mg., score bottles of 100 and 500 tablets and cartons of 100 tablets in 1 strips.

For additional product information, consult the package ins or see your Upjohn representative.

MED B-1S (KC

Upjohn The Upjohn Company, Kalamazoo, Michigan 49001

Deltasone® 5 mg. (prednisone, Upjohn

an economical prednisone that's made a name for itself

A once-popular treatment for back pains was to have the seventh son of a seventh son stand or walk on the patient's back.

The pain of earache was allegedly relieved by holding a hot roasted onion to the ear.

For headache, a sovereign remedy was to wear a snakeskin round one's head.

A realistic approach to pain relief

'Empirin'®

Compound with Codeine Phosphate gr. 1/2 No. 3

Each tablet contains:
Codeine Phosphate gr. 1/2 (Warning—May be habit forming), Phenacetin gr. 2 1/2, Aspirin gr. 3 1/2, Caffeine gr. 1/2.

keeps the promise of pain relief

'B.W. & Co.' narcotic products are Class "B", and as such are available on oral prescription, where State law permits.

BURROUGHS WELLCOME & CO. (U.S.A.) INC.
Tuckahoe, N.Y.

The actions of the official Tincture and Extract of Belladonna result chiefly from their Atropine content . . . conclude Goodman and Gilman

THE PHARMACOLOGICAL BASIS OF THERAPEUTICS
3rd Edition, page 522

ANTROCOL®

Antrocol provides the prompt, predictable antisecretory action of the belladonna alkaloid, atropine, fortified with sedation and blended with Bensulfoid, contributing to even absorption.

Each tablet or capsule contains: Atropine sulfate, 0.324 mg.; Phenobarbital, 16 mg. (may be habit forming); Bensulfoid, 65 mg. (see white section PDR). The atropine content of Antrocol is the maximum amount the average patient can take at six hour intervals over long periods with comfort.

SUPPLIED
Tablet in bottles of 100, 500 and 5000
Capsule in bottles of 100, 500 and 1000

Caution: Federal law prohibits dispensing without prescription.

PRESCRIBING INFORMATION

Contraindicated in glaucoma. Use cautiously in prostatic hypertrophy. Side-effects of toxic dose of atropine: flushing, dryness of mouth, cycloplegia, tachycardia and urinary retention.

DOSAGE: One tablet or capsule after each meal to correct emotional stress and normalize gastric secretions. In treating peptic ulcer, doses at regular intervals up to eight (8) tablets or capsules per day to provide the proper gastric titer for healing. After ulcer has healed, one tablet or capsule after each meal to maintain a titer unfavorable to recurrence.

Clinical supply available to physicians.

WILLIAM P. POYTHRESS & CO., INC.
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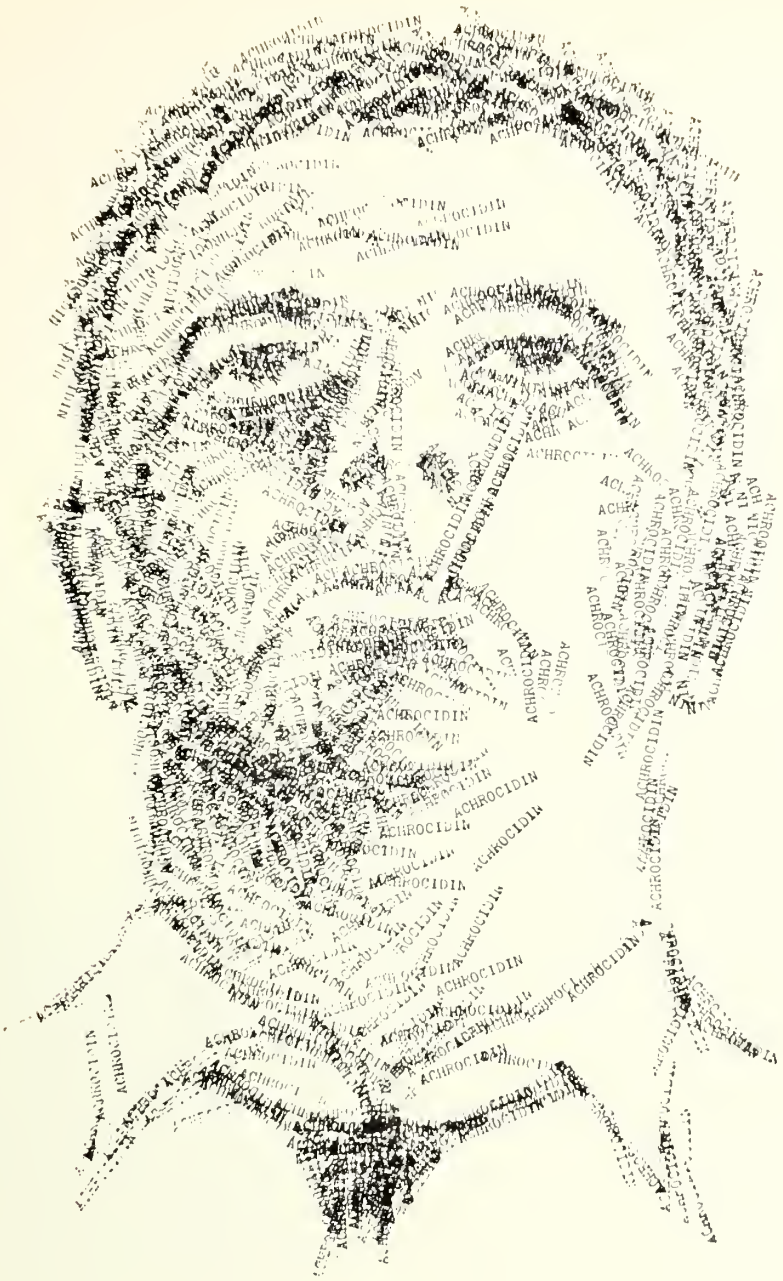

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THE JOURNAL *of* The Maine Medical Association

VOLUME 61 DECEMBER 1970 NUMBER 12

Eastern Maine Medical Center Number

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The Journal of The Maine Medical Association

Published monthly at Brunswick, Maine, under the direction of the Council

DANIEL F. HANLEY, M.D., *Editor* PATRICIA A. BERGERON, *Business Manager*

The JOURNAL assumes no responsibility for opinions and statements of contributors. All copy, original articles, case reports, etc., should be submitted for publication typewritten on standard size paper and double spaced. Proof sheets furnished author on request. Address, P. O. Box 250, Brunswick, Maine 04011.

Reprints

Communicate at once with the Business Manager if reprints are wanted.

Entered as second-class matter December 22, 1926, at the post office at Portland, Maine, under the act of August 24, 1912. Second-class privileges authorized at Brunswick, Maine.

Subscription price to members $6.00 per year.

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Neurologic Manifestations of Infective Endocarditis

Joe R. Wise, Jr., M.D.*

**"Things aren't always what they seem.
Skim milk masquerades as cream."
W. S. Gilbert**

"It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future."[1]

With this introduction, Osler began his lecture on Malignant, Endocarditis delivered to the Royal College of Physicians in 1885.

In the intervening years, infective endocarditis has continued to evoke widespread interest among clinicians. Of all the prolonged febrile illnesses, it has been one of the most challenging as an exercise in diagnostic acumen.

The site of the infection is impalpable and cannot be visualized even with the most modern diagnostic techniques. The cardinal signs – fever, heart murmur and a petechiae – may often be caused by other diseases or they may all be absent in endocarditis. Finally, the nature of the embolization is such that lesions may be produced in any organ and may readily simulate other disorders.

Of special interest in this regard, from the standpoint of diagnostic intrigue, are those patients with endocarditis who present with seemingly well defined syndromes which direct one's attention away from the heart.

The central nervous system is frequently involved in the course of many well known diseases in which the primary process is far removed from the brain, and of all these diseases, infective endocarditis is one of the most pressing importance.

Osler, in his Gulstonian Lectures, first called attention to the features of endocarditis and stressed its importance as a clinical entity. He pointed out that frequently, complicating embolic lesions may occur in the brain substance or in its covering membranes. He found that these embolic softenings, either bland or suppurative, were extremely common in the cerebral hemispheres and that they could occur as a single focus with extensive suppuration and resulting paralysis of one side of the body, or as multiple small infarcts.

Many detailed studies followed which confirmed these neuropathological aspects. Kimmelsteil,[2] in 1927, made a thorough pathological investigation of the brain lesions in cases of bacterial endocarditis and found inflammatory lesions in a large majority. The outstanding and most characteristic change noted by him was a diffuse embolic encephalitis showing no predilection for any single portion of the brain substance. There was much mention in the literature of that period of this so-called "viridans encephalitis."

DeJong, in 1937, reported emboli and thrombi in cerebral vessels, subarachnoid and inter-ventricular hemorrhage, brain abscess and mycotic aneurysm, in patients dying of endocarditis.[3]

The fundamental pathological change in the central nervous system in cases of subacute endocarditis is a diffuse, embolic meningo-encephalitis and from this the manifold clinical manifestations arise. In acute endocarditis due to pyogenic organisms, involvement of the brain is also common; however, it is more often accompanied by sepsis, of both the brain and meninges with abscess formation.

Much has been written concerning the neurologic dysfunctions that result from these lesions that so frequently accompany endocarditis, and their clinical manifestations were noted from the early descriptions of the disease. The incidence of such involvement in numerous series[3–19] varies around 30%; compare this with the gen-

*From the Medical Service, Eastern Maine Medical Center, Bangor, Maine 04401.

eral clinical incidence of splenomegaly which is about 50%.

Since the types of lesions are pleomorphic and no local area of the brain substance appears immune to injury, the consequent neurologic manifestations are varied and not altogether predictable. The neurologic disturbances produced may be sudden or gradual in onset, may be relatively unimpressive, or may dominate the clinical picture completely and suggest, for months, such a variety of diagnoses as dementia, tumor of the brain or multiple sclerosis.

Many patients have been referred to the hospital for reasons quite foreign to the real issue and some followed devious channels before being successfully diagnosed.

In one series, one patient was referred as a right frontal lobe tumor, another came from a distance of 500 miles for the repair of an old skull fracture and a third came for psychiatric evaluation because he was accusing his fellow prisoners of poisoning his food. Still another was rushed in by excited friends after the occurrence of a convulsive seizure, and a fifth patient descended on an unsuspecting house staff with a left hemiplegia and aphasia.[3]

As a consequence of the wide spread participation of the brain, the neurologic manifestations are extremely varied. There does emerge, however, a broad pattern to which these signs adhere.

Headache is one of the most common symptoms of this disease and it may be one of the earliest. All authors comment on the frequency of this rather non-specific symptom and in some series it occurred in 25% of cases and was the most frequently encountered neurologic symptom. The headache, of course, may be only the result of the generalized toxemia, or it may occur during the embolic phase of the disease and signify meningitis, brain abscess, or cerebral infarction.

Focal embolic brain lesions are a dramatic and important part of the pathologic anatomy of endocarditis and frequently produce the outstanding features of the syndrome. A variety of neurologic defects may be produced in this manner and one of the most common is hemiplegia, a symptom complex which is present in as many as 30% of patients with endocarditis who manifest CNS symptoms.

Several authors emphasize this occurrence. In Krinsky's review of 100 cases of endocarditis from Boston City Hospital, hemiplegia or hemiparasis was the most frequent neurological sign, occurring in 31% of his cases.[13] Thirty-five percent of the 442 cases reviewed by Cates and Christie sustained a major arterial embolism in life, and over half of these were cerebral, tending to develop shortly after therapy was begun.[6] But they emphasized as well that, not only did some patients present with hemiparesis, but that the risk of a major embolism remained real for several months (8-20) after apparent cure. In a number of series, cerebral embolism was, with heart failure, the leading cause of death.

Jochmann's maxim states that "in young adults with hemiplegia always think of bacterial endocarditis." This maxim may be extended to all age groups. This manner of presentation may be particularly misleading in older persons where the hemiplegia is usually attributed to cerebrovascular thrombosis rather than embolism . . . especially when there are no other characteristic features of valvular infection. It is of particular interest in this regard that many of the patients with endocarditis who presented with strokes were over the age of 50.

As was duly emphasized by several authors, the occurrence of stroke and concomitant meningitis was particularly suggestive of endocarditis.

Even more striking than hemiplegia is the diagnostic difficulty in those patients with endocarditis who appear to have meningitis or meningo-encephalitis . . . as is vividly demonstrated by the following case.

Case Report

W. F., a 31-year-old man, was transferred from a neighboring hospital where he presented with fever and a stiff neck.

He was employed as a freight handler and enjoyed good health until 2 weeks prior to his admission when he developed a headache. He was referred to a local physician who informed him that he had an infected tooth. One week before admission he consulted a dentist who removed the tooth and gave him one injection (100 mgms) of Terramycin®. The headache, which had never abated, within two days was accompanied by nuchal rigidity, fever, sweats and malaise. He tried to work but because of the above symptoms returned home where he remained until his admission. The family reported that he was disoriented but remained generally quiet without convulsions. There was no history of antecedent rheumatic fever.

He was taken to a hospital where a lumbar puncture was performed. The spinal fluid was cloudy and contained 98% polys. The protein was 36 mgms% and sugar 54 mgms% at a time when the blood sugar was 90 mgms%.

Physical examination revealed an acutely ill man who appeared very lethargic. He was oriented but responded slowly to questions and commands. His temperature was 104° and the blood pressure was 140/60. The right cornea was scarred from an old accident. There were no hemorrhages in the fundus or conjunctivae. There was nuchal rigidity and the Kernig sign was present. The tympanic membranes were infected and slightly opaque but were not bulging. The heart was not enlarged and the rhythm was normal. There was a grade ii/vi systolic murmur in the 3rd left intercostal space, a grade iii/vi blowing decrescendo murmur along the left sternal border and a diastolic "noise" at the mitral area. No spleen was palpable. There was no rash and no embolic phenomena. The neurologic exam, except for the clouded sensorium, was normal.

The hemoglobin was 13.5 and white count 19,100. Skull x-rays suggested left frontal sinusitis.

A repeat lumbar puncture was performed and yielded 776 WBC (74% polys). The sugar had fallen to 46 mgm% (Blood sugar 100 mgm%). Bacterial smear was negative.

Six hours later the lumbar puncture was repeated. On this occasion there were 776 WBC's (86% polys) and the CSF sugar was 36 mgm%. Penicillin was begun.

By morning the diastolic "noise" had developed into a rumbling murmur, the aortic diastolic murmur was louder and the diastolic blood pressure hovered around 50 mm Hg. Streptomycin was added.

By the 3rd hospital day pneumococci were isolated from the blood culture and the Streptomycin was discontinued. A brain scan was normal. By the 6th hospital day, he was absolutely afebrile and remained so the remainder of his 36 day hospital course.

Spinal fluid cultures were sterile.

He was discharged in an asymptomatic condition with a blood pressure of 120/60 to be followed in Cardiology Clinic.

Meningitis was noted as a clinical manifestation of endocarditis from the very early descriptions of the disease. Osler made several distinct references to such occurrences and pointed out that "the meningeal complications of endocarditis have not received much attention."[1] In Toone's review, of all the clinical manifestations of CNS damage, meningitis appears the most frequent. In varying degrees of severity it was noted in 11/17 cases, and was most severe in cases of acute endocarditis.[15] Often the meningitis was present in conjunction with other neurologic changes such as subarachnoid hemorrhage, intra-cerebral hemorrhage and hemiplegia and this combination of lesions was particularly significant.

The spinal fluid changes, present in all cases of meningitis were generally divided into two broad groups. In cases of subacute endocarditis, although emboli deposited in the meninges contained organisms, and these bacteria were frequently visible in stained smears of the spinal fluid, they usually failed to grow when culture was attempted. Polymorphonuclear leukocytes usually formed the most part of the cellular response and numbered in the hundreds. In only a small number of cases of endocarditis, however, has S. viridans ever been cultured from the spinal fluid. This fact seems highly significant and should lead us to make a very close and thorough investigation for the presence of viridans endocarditis in all patients with so call "sterile meningitis." Since fungal or viral or partially treated bacterial infection of the meninges is the most common cause of this syndrome, the association with endocarditis is not often considered.

Since the viridans steptococcus is not a pyogenic organism, complicating brain abscess in subacute endocarditis is a rare event, the cerebral lesion usually being limited to infarction. In acute endocarditis, on the other hand, especially when due to the Staphylococcus or Pneumococcus, embolization of the brain often results in purulent meningitis with thousands of cells, and in these cases single and even multiple brain abscesses are the rule. The offending organism can almost always be recovered from the spinal fluid.

In infective endocarditis, the psychiatric symptomatology is often rich and prominent and indeed may so color the picture that the total situation may escape the observer for weeks. Prominent neuropsychiatric symptoms were described in over 50% of the cases of endocarditis 30 years ago, and continue to cause diagnostic confusion, especially in the older persons. Electroshock has been mistakenly administered. These emotional disturbances may occur in both types of endocarditis, but particularly in the subacute form they may alone comprise the most prominent symptoms.

In most series, mental symptoms were prominent in 20% of cases and were variously diagnosed. Impairment of consciousness in degree from somnolence and inattentiveness to coma was common and would not be unexpected in most serious illness. Convulsions were frequent.

In a disturbingly large number of cases, however, the outstanding symptom was listed as delirium, restlessness or depression. A few cases of frank hallucinations and psychotic behavior were recorded. The similarity of many of these symptoms to those of functional disease is apparent and was often the cause of difficulty in diagnosis. Consider the following examples:

A man of 53 became ill 6 months before admission with symptoms of increasing fatigue and depression.. Two months later he collapsed and was put to bed with a "nervous breakdown." He became increasingly weak and was prone to fits of weeping, especially when talking to strangers. Although other symptoms were present, they escaped recognition because of the predominant mental symptoms.

An 81-year-old man was referred to the hospital because he had suddenly become confused, noisy and belligerent and had threatened to kill his wife. After he was subdued by police, he was brought to the hospital and put in a locked room in the psychiatric ward. He had a temperature of 99.5, a systolic apical murmur and no other physical abnormalities.

A 67-year-old man was admitted because of weight loss and depression. On admission, he was depressed and uncommunicative. From his family, it was learned that he had suffered occasional periods of periodic moodiness but for the past two weeks he had not stirred out of his room and had passed the time gazing at the wall. His temperature was 99° and there was only a faint systolic murmur.

A 45-year-old man was admitted complaining of double vision and generalized weakness. He was confused, disoriented and hallucinating actively in the visual and auditory spheres. He was afebrile.

In one young boy, the disease was manifest by a striking disorder of behavior. He tripped his mother, made sudden attacks on strangers and generally provoked others with his extreme insolence.

All had established endocarditis and the treated cases who survived returned to normal behavior.

Aside from these larger general groups of symptoms, meningitis, stroke, emotional disorder, the variety of CNS malfunctions produced by endocarditis are legion. Visual disturbances are common and may include; retinitis, optio neuritis, papilledema, blindness of embolic origin, field defects or interruption of the tracts in the brain substance. Paralysis of the extraocular muscles, the face, the palate, the larynx and tongue have occurred. There may be tremor, focal or general convulsions, ataxia, aphasia, and vertigo. Chorea has been described, as have such various parakinesias as scratching movements and Parkinsonism, Dyskinesias were expressed as persistent chewing movements, rhythmic protrusion of the tongue and myoclonus of the extremities.

In short, the whole of neurology may be represented, and, when it is considered how these lesions are produced, this is not at all surprising.

In the past, writers have emphasized that one of the difficulties in the diagnosis of endocarditis has been the similarity of symptoms of endocarditis to those of everyday illness, especially in the elderly patient in whom the

symptoms may be unusually atypical and vague.[12] It is being increasingly appreciated that, in contrast to the usual fevers of undetermined origin, many patients present with what appears to be a well defined cause for their fever and one which would direct attention away from the heart.

Osler pointed out that "a considerable number of patients come under observation for the first time with symptoms of cerebral or even cerebrospinal trouble." Most recent reviews of infective endocarditis while emphasizing the incidence of neurologic complications, have failed to stress how frequently the latter form the presenting clinical picture. Since endocarditis has such a high incidence of neurologic symptoms, and since these symptoms are not infrequently the first to occur, their recognition may lead to the impression that the primary lesion is in the nervous system and hinder rather than aid in arriving at the diagnosis.

In one large series, 30% of the cases of endocarditis were admitted to the hospital with one or more neurologic manifestations. In 20% of these cases, the signs and symptoms were so predominantly neurologic that the primary lesion was thought to be in the CNS.[13] Six of DeJong's cases were admitted to the hospital for the evaluation of their neurologic manifestations which varied from meningo-encephalitis to CVA.[3]

There is a recent review from an English hospital of 33 cases of endocarditis that presented a problem in neurologic diagnosis at the time of admission. In these cases, the neurologic features were the direct cause of their hospital admission and posed the initial diagnostic problem. In 22 of these cases, 66%, neurologic symptoms preceded the onset of all others.[18]

It should be mentioned at this point that, almost without exception, patients with subacute endocarditis had heart murmurs at the time of their initial examination.[9] With acute endocarditis, produced by pyogenic organisms which are capable of attacking normal heart valves, murmurs were sometimes absent in the early stages of the disease, but nearly always developed in patients who survived.

It is worthy of emphasis, in summary, that embolism of the brain and cerebral vessels is as integral a part of endocarditis as are the embolic lesions of other structures, and the resulting neurologic symptoms and signs merit equal importance with the murmur, fever, and enlarged spleen in the constellation of this syndrome.

Since the diagnostic consequence of this disease are so far reaching, endocarditis should be considered as a differential possibility when patients are admitted with neurological complaints, since these manifestations may be the earliest evidence of its existence.

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A Medical-Surgical Clinic Service in a Mental Hospital

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Does being a patient in a mental hospital automatically render a person immune to all physical disease? Certainly not, we would quickly reply. Nevertheless, the problem that has for many years plagued mental institutions in our country is the problem of detecting and managing the physical illnesses of psychiatric patients. Being acutely aware of the lack of medical attention for this kind of patient, many mental hospitals in recent years have organized Medical-Surgical Services to care for the organic diseases of their psychotic patients.

When detection and care of physical illness is left solely to the psychiatric staff, the mental patient is denied the right to receive the best possible treatment both of his mind and body. The function, then, of a Medical-Surgical Service in a mental hospital is to assist the psychiatrist and the psychiatric ward personnel in caring for patients with acute and chronic medical illnesses. Utilizing well-trained personnel and specialized equipment, the Medical-Surgical Service can provide a high quality of medical treatment and patient care.

STRUCTURE OF THE MEDICAL-SURGICAL SERVICE IN THE BANGOR STATE HOSPITAL

The organization and structure of a Medical-Surgical Service is generally determined by the specific needs of each individual hospital and the availability of physicians to staff such services. In November of 1969, the Medical-Surgical Unit of the Bangor State Hospital was opened with an initial staff of one physician, two registered nurses, six licensed practical nurses and five psychiatric aides. The Medical-Surgical Unit, having a maximum in-patient capacity of twenty-one beds and serving a hospital population of about twelve hundred patients, serves as the nucleus of a Medical-Surgical Service. In December, 1969, an Outpatient Medical-Surgical Service was initiated to provide both preventive and therapeutic medical care for the patients in Bangor State Hospital. This service, in the form of a Medical-Surgical Clinic, serves to organize and coordinate all Medical-Surgical activities in the hospital.

The clinic is located in a small area of the hospital, close to the Medical-Surgical Unit, but yet isolated from all the wards to provide a quiet atmosphere. The physical plant consists of a hallway (functioning as a waiting room), two examining rooms, and a bathroom. One registered nurse, working a forty hour week, Monday through Friday, comprised the initial nursing staff of the clinic. Acting as consultants for Bangor State Hospital, several physicians from the Bangor community provide services weekly at designated times. The beginning services offered by the clinic were a Medical-Surgical Clinic, an Orthopedic Clinic, a Gynecological Clinic, and an Employee Clinic. In June of 1970, a licensed practical nurse was added to the staff to serve as the clinic assistant.

FUNCTION OF THE OUTPATIENT CLINIC

The clinic serves as a type of filtering system through which patients are (1) recommended for admission to the Medical-Surgical Unit, (2) referred for consultation to a community physician, or (3) given recommendations for treatment and returned to the psychiatric service. Patients who are returned to their resident wards following discharge from the Medical-Surgical Unit are followed as necessary in the clinic.

The clinic also functions to provide a diagnostic and preventive medical care for patients. A physiological screening program, includes annual chest x-rays, urinalysis, CBC's, 2-hour postprandial blood sugars, and PAP smears. The RN Clinic Nurse, under medical supervision, performs pelvic examinations, breast examinations, pap smears, sigmoidoscopies, routine foot care, and administers immunizations. In addition, EKG's and Tonometries in persons over 40 years are performed. The clinic personnel make periodic rounds of all wards, carefully observing patients for any sign of impending illness. An important factor in preventive medicine is the education of ward personnel. Teaching is generally done on an informal basis when the opportunity arises.

The clinic also provides services for employees. All applicants for employment receive a physical examination and a chest x-ray, urinalysis, and serology. For ill or injured employees, the clinic provides emergency treatment. Annual Tine tests, annual chest x-rays, smallpox vaccinations, and Diphtheria and Tetanus immunizations are available to employees.

STATISTICAL DATA DURING A NINE MONTH PERIOD IN THE CLINIC

During the first nine months of operation the clinic has seen approximately 1,500 patients and employees for medical treatment or service (see Table 1).

A total of 42 patients entered the Eastern Maine Medical Center or St. Joseph Hospital for surgery.

Seventy-three patients were seen by consulting physicians in their offices. Through the clinic other services in the community have been utilized by patients, such as the tumor and hematology clinics and the radiotherapy department at the Eastern Maine Medical Center.

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TABLE 1

Clinic	*No. of Pts. Seen*	*Numerical Breakdown of Pathology*
Medical-Surgical	410 patients	355 varied medical problems 55 surgical problems
Gynecological	320 patients	3 surgical D & C's 2 hysterectomies 290 PAP smears done yielding 2 Class IV (conclusive for malignancy) and 1 Class III (suggestive of malignancy)
Orthopedic	96 patients	20 hip fractures 9 back conditions 8 tibia and/or fibula fractures 5 wrist fractures 7 fractures of the humerus 4 clavical fractures 3 ankle fractures 3 fractures of the patella 5 fractures of the metacarpals or metatarsal 13 other conditions
Employee	313 patients	200 new employees 113 sick or injured employees
Sigmoidoscopy	100 patients	12 hemorrhoids 5 polyps 1 enlarged prostate gland 1 rectocele

DISCUSSION

Medical problems in mental hospitals have always existed, and medical neglect has been an all too common occurrence in these institutions. At Bangor State Hospital, ward personnel have been handicapped for many years by the knowledge that no organized help was previously available for their patients. During the nine months of the clinic's operation, numerous medical-surgical problems were detected and treated. These problems, for the most part, were not unlike those seen in the non-institutionalized community, but the mode of presentation was often different in that patients with acute surgical illnesses and cardiovascular catastrophies appeared without classic complaints. One patient who offered no complaints was observed by the staff to have had "a change for the worse." Further investigation revealed the presence of shock, atrial fibrillation, and EKG changes of acute anterior myocardial infarction. Without an alert staff, this patient's cardiovascular catastrophe most probably would have gone undetected.

Malignancies were difficult to detect and thus prompted a vigorous cancer detection program within the institution. Three patients were admitted to the hospital with the diagnosis of depression. This diagnosis was based on the presence of a flattened affect, slowing of intellectual processes, and psychomotor retardation. Associated weight loss and other symptoms were attributed to somatic expressions of depression. Medical evaluation of these three patients revealed the presence of carcinoma of the esophagus, carcinoma of the stomach, and carcinoma of the lungs with metastasis to the pericardium with pericarditis. There was little to offer these patients at the time of diagnosis; however, it is significant that two of these patients had been present in the institution for a period in excess of one year.

Two cases of basal cell carcinoma, a lesion well known for its good response to radiotherapy, were present in the institution for more than two years before diagnosis and treatment was rendered.

The common denominator of these patients was their inability to present well known medical illnesses in a manner that was recognizable to the staff and their inability to insist on diagnosis.

The foundation of any delivery system for medical care is a well-organized, well-trained, highly motivated staff. In view of the scarcity of medical manpower, and the low priority given to care for the chronically and mentally ill by health planners, utilization of nursing personnel as medical assistants under medical supervision seems prudent.

Our experiences in these areas thus far have been most gratifying as evidenced by the yield of our sigmoidoscopy and pelvic examination programs. These programs are completely run by trained nursing personnel under medical supervision.

The educational value of the availability of medical care to the entire staff became increasingly more evident as months passed. This was best noted in the improvement of the staff utilization of the clinic facilities. The caliber and promptness of medical referrals steadily improved and increased, and the nursing staff, with primary psychiatric responsibility, increasingly sought information concerning medical problems. The clinic's effect was also noted beyond the institution in the medical community at large by the physicians who were utilized as consultants and for the first time were working within the institution on a concentrated basis. Consultants became easier to obtain and worked in a motivated manner previously not apparent from examination of the hospital record. This experience has been most rewarding for patient, institutional staff, and community physician consultant.

The future holds a challenge to the medical and paramedical personnel of the Bangor State Hospital in striving to improve and increase the quality of medical care rendered to each patient in this institution. Essential to meeting this challenge is the development of an inservice education program that stresses the concept that the patient is a total human being with physical, mental and social needs. This comprehensive approach along with the development of techniques that foster communications within the hospital complex between staff members and between employees and patients represents the foundation of an inservice education program.

CONCLUSION

Nine months experience of a medical-surgical outpatient service in a 1,200 bed mental hospital has been pre-

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Iodide Induced Myxedema: A Failure of Autoregulation

"What One Knows, One Sees"
— Goethe

JOE R. WISE, JR., M.D.*

The development of myxedema is an unusual complication of the prolonged use of iodides. Fewer than 20 cases of iodine induced myxedema have been reported in the English literature even though large numbers of patients take iodides for asthma and other chronic lung diseases. Included below is the description of a patient who developed severe myxedema while taking an iodine containing preparation for chronic bronchitis (Quadrinal®).

CASE HISTORY

A 60-year-old retired carpenter, was brought to the Emergency Room by a friend who, after trying unsuccessfully to contact him by phone, found him at home fully dressed, slumped over a table and difficult to arouse. On arrival in the Emergency Room, he was somnolent but arousable, and his respirations were normal. His pulse was 48-56. Electrocardiogram showed "bradycardia, nodal rhythm." Little history was available except that he may have had a myocardial infarction 3 years previously and had some sort of lung disease for which he was taking an aminophylline-type medicine and digitalis.

In the Intensive Care Unit, he appeared to be asleep. He was arousable and once aroused, he was cheerful and cooperative as long as he could keep awake. He was oriented but his speech was slurred and his voice hoarse. His skin was sallow and although he was thin, his eyes were puffy. No thyroid was palpable. His chest was hyperresonant with an increased AP diameter and distant breath sounds. There were tobacco stains on his fingers. The skin was exceedingly dry with large flaking areas, and there were heavy keratin deposits over the elbows, knees, and feet. He was very weak and could stand only with assistance. His reflexes were symmetrical but their return was slowed considerably. There was a fairly marked hearing loss. The heart was small. The rectal temperature was 97°. An esophageal electrocardiogram lead was placed and demonstrated p-waves and a sinus bradycardia of 40-50 min.

The family arrived to report that his general health had been good, interrupted only by an accident and an appendectomy. Four years ago he had retired from carpentry and had worked at odd jobs where he felt generally well but fatigued easily. Two years ago he had a "heart attack" and since then had been taking digitalis (Gitalin® 0.5 mgm./da), Dramamine® for dizziness and Quadrinal® for respiratory difficulty.

Although there had been no acute change for the past year, he seemed to become progressively weaker to the extent that occasionally he could not stand alone. His mental facility and movements had slowed remarkably. His hearing had become so bad that he had resorted to putting the telephone on a bucket so he could hear it ring. He was constipated and complained of it. In addition, he complained that the cold bothered him severely and he kept his house so warm that it was intolerable to his relatives who would refuse to visit him for this reason, except on the coldest days.

A transvenous demand pacemaker was inserted, digitalis was discontinued and thyroxine (.025 mgm/da) and cortisone were begun. Serum sodium was 142 meg/1, arterial pCO2-42 meg/1. Rectal temperature rose, his heart rate increased, and he became more alert. Within 24 hours, he developed a temporary but alarming paranoia and restlessness, both of which seemed to disappear as the dose of steroids was tapered. Tests done on admission: PBI – "contaminated," T4 by column – 2.4 (2.9 -6.4), plasma corticone (PM) 27.6 mgm %, cholesterol 390 mgm%, sella size was within normal limits. After 10 days of thyroxine q.o.d. (.025 mgm.) an RAI uptake was 6% in 24 hrs.

He improved very rapidly, his spirits brightened, and his movements quickened so that within only two weeks, by the family's account, he was perfectly normal.

After 18 days of treatment (10 days .025 mgm. thyroxine qod, 8 days .050 mgm. thyroxine qod), repeat PBI was 11 mgm % and RAI was 58%. Thyroid was stopped. Two attempts to demonstrate iodine induced block were technically unsuccessful and a T3 suppression has not been done.

After 15 months, he remains euthyroid without medication and is active enough to complain of claudication.

Iodine induced myxedema was described for the first time in 1928 in a young woman who was being treated with iodine for a post-operative recurrence of Graves disease.[1] Others have described the occurrence of myxedema after administration of iodides to patients who had pre-existing non-toxic goitres and there are reports of several patients who have developed iodine induced myxedema and then hyperthyroidism in different periods of life.[2] Recently, Paris[3] reported 5 patients with no known disease of the thyroid who developed myxedema while taking iodides for the treatment of asthma or chronic bronchitis.

Many drug mixtures used in the treatment of chronic lung diseases contain iodine and patients with these diseases may take doses of iodine far exceeding their daily requirements for many years. It is surprising then that occasionally one of these patients should develop myxedema. Moreover, the myxedema seems to be caused by the iodine since, as soon as its use is discontinued, the myxedema disappears.

Iodine is concentrated in the normal thyroid gland by an energy dependent system referred to as the "thyroid pump." Once concentrated this iodine is available for organification and, ultimately, incorporation into thyroid hormone.

Anti-thyroid drugs such as methimazole and propylthiouracil block the organification of the trapped iodine and no hormone is formed. Since the iodide concentrating mechanism, or the "thyroid pump," is not inhibited by these anti-thyroid drugs, this non-hormonal inorganic iodide continues to accumulate in the gland.

Perchlorate however, will inhibit the "pump" and

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under these circumstances the inorganic iodide which has been concentrated will reflux back into the blood until the concentration in the blood and the thyroid are again the same. This procedure then, the perchlorate discharge, provides a way to demonstrate this blocked organification which can be induced by anti-thyroid drugs.

This block in organification can be caused by iodides as well as anti-thyroid drugs and this iodine block was best demonstrated by Wolff and Chaikoff[4] (the Wolff-Chaikoff effect). They showed that high concentration of serum iodine blocked thyroid synthesis by blocking organification, just as propylthiouracil, and that thyroid synthesis resumed as plasma levels of iodine declined. Thyroid iodine uptake increased initially and varied directly with the serum level, provided these levels were relatively low, but with high serum concentration a critical uptake of iodine was reached and organification was blocked.

This block constitutes an intra-thyroidal regulatory mechanism with small increments of iodine, trapped iodine reaches a critically high level, organification of iodine is blocked and the synthesis of hormone is decreased. This is the basis on which Lugol's solution is given to patients with hyperthyroidism. After a time, however, normal individuals "escape" from this iodine induced block, probably the result of a compensatory decrease in iodine uptake until the concentration of iodine within the gland falls and the block is relieved.

In patients with iodine induced myxedema, therefore, the abnormality is not only an inhibition or block of organification but a failure to "escape" from or "adapt" to this iodine induced block and thyroid synthesis remains blocked as long as the iodine concentration in the blood remains high.

It is not known why only a small number of patients who take iodides for prolonged periods should develop myxedema. Some feel that these patients are unusually susceptible to the inhibitory or blocking effect of iodine. In some of these patients the iodine uptake of their thyroid cannot be suppressed by triiodothyronine (T3), an abnormality most commonly encountered in patients with thyrotoxicosis. This failure of suppression by T3 suggests either autonomous secretion of thyroid stimulating hormone (TSH) by the pituitary or autonomous function of the thyroid itself.[5]

The mechanism of iodine induced myxedema seems most closely related to this autonomous function. As the serum level of iodine rises, the secretion of thyroid hormone increases commensurately. Normally there is a compensatory decrease in TSH secretion and a fall in the iodine uptake. In these patients with iodine induced myxedema, however, because of autonomous function of the thyroid or pituitary, the uptake of iodine continues and it accumulates to the point that organification is blocked. With thyroid synthesis blocked, the level of circulating thyroid hormone falls and myxedema ensues.

In summary then, some patients develop myxedema when exposed to prolonged iodine treatment. Many of these patients are taking iodide containing drugs as treatment for chronic lung disease. It appears that the basic abnormality in these patients is the inability of their thyroid gland to stop taking up iodine when large amounts are available, the result of autonomous function of either the thyroid or the pituitary. Iodine accumulates within the gland and reaches a concentration high enough to block the organification of iodine, thyroid hormone synthesis is impared and myxedema develops.

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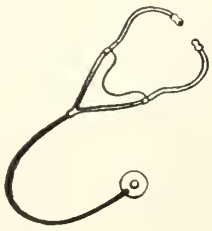

Percutaneous Transhepatic Cholangiography

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Within recent years, numerous reports have appeared in the literature[1-11] describing the technique and results of percutaneous transhepatic cholangiography as a diagnostic aid in the evaluation of the jaundiced patient when clinical and laboratory data suggest an obstructive etiology. The differentiation between intrahepatic and extrahepatic biliary obstruction is at times quite difficult, and any procedure or diagnostic maneuver which might be helpful in making this differentiation would be welcome. In addition, when extrahepatic obstruction is found to be present, the localization of the obstructing lesion may be of real value to the surgeon.

The following report presents the application of this technique in the diagnosis and management of several patients with obstructive jaundice together with a discussion of the reported experience of others with this procedure.

METHOD

Prerequisite for undertaking percutaneous transhepatic cholangiography is the presence of a normal prothrombin time, platelet count, and bleeding time. The procedure is contraindicated when the prothrombin time is abnormal and does not return to the normal range after the parenteral administration of vitamin K on three successive days. A broad spectrum antibiotic such as ampicillin or tetracycline should be given prior to, and for at least one day following, the procedure in order to lessen the possibility of septicemia. In addition, an analgesic such as meperidine may be given immediately before the procedure. The patient is then taken to the Radiology Department and placed in the supine position. Two approaches to the liver have been described: the mid axillary line is used by some, and the mid clavicular region below the right costal margin is utilized by others. The latter approach has been used in the patients to be presented in this study.

After Xylocaine® infiltration of the skin and subcutaneous tissue and under fluoroscopic control, a 15 cm 20 gauge needle or a No. 18 Teflon catheter with a 19 gauge stylet is introduced at a 45 degree angle and directed posteriorly and medially utilizing air in the duodenal loop as a landmark. The needle is then withdrawn until bile can be aspirated signifying entrance of the needle tip into a bile duct. This bile may be sent for culture and cytological examination. After the removal of as much bile as possible, a radio-opaque material such as 50% Hypaque® or 60% Renografin® is then introduced in order to fill the biliary tree and extrahepatic bile ducts. Appropriate radiography in various projections may then be obtained for interpretation and documentation.

Fig. 1 – Case 1. Normal size common bile duct and intrahepatic biliary tree with well filled gallbladder. Note the presence of contrast material in the duodenum indicating patency of the common duct.

REPORT OF CASES

Case 1 – A 53-year-old white male was well until two weeks prior to admission when he noted the onset of dark urine, light colored stools and jaundice of the skin and sclerae. This was associated with mild anorexia but there was no history of nausea, vomiting, pain or weight loss. Over the proceeding nine years, the patient had twice been admitted to the hospital with a diagnosis of acute pancreatitis on each occasion. He had a history of moderately heavy alcohol intake for at least fifteen years.

Physical examination on admission revealed the patient to be deeply jaundiced, alert and oriented. The abdomen was soft, and an enlarged, slightly tender liver was palpated to extend 10 cm below the right costal margin. The spleen was not felt and the remainder of the examination was normal.

Laboratory studies revealed the following values: hematocrit, 30%; WBC, 13,200 with 78% segmented neutrophiles; sedimentation rate, 125mm per hour; serum electrolytes: sodium 129 meq/L, potassium 3.8 meq/L, chloride 97 meq/L, CO_2 22 meq/L, alkaline phosphatase, 135 I.U./L; SGOT, 43 I.U./L; SGPT 12 I.U./L; serum bilirubin, 30.8 mgms% (18.5 mgms% direct); serum protein, BUN, creatinine, FBS, amylase, lipase, prothrombin time, calcium, phosphorus, and urine analysis were normal. Chest x-ray revealed left venticular enlargement and a plain film of the abdomen revealed hepatosplenomegaly. There was no evidence of pancreatic calcification. An upper GI

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Fig. 2 – Case 2. Complete obstruction of the common bile duct with dilatation of the intrahepatic biliary tree. Gallbladder is noted to be partially filled.

Fig. 3 – Case 3. Markedly dilated common bile duct and intrahepatic biliary tree with complete obstruction of the common bile duct. Note dilated cystic duct and partial filling of the gallbladder.

series was essentially normal except for displacement of the stomach and duodenum due to an enlarged liver.

The laboratory studies were consistent with a diagnosis of obstructive liver disease. Obstruction due to calculus, tumor, or pancreatitis appeared likely, but a diagnosis of "alcoholic hepatitis" with cholestasis could not be excluded. Accordingly, exploratory laparotomy preceded by percutaneous transhepatic cholangiography was planned. The patient was taken to the Radiology Department, and under local anesthesia, a PTC was carried out. This study revealed the presence of a normal size common bile duct and intrahepatic biliary tree without evidence of obstruction and the free flow of bile through the common duct into the duodenum. No evidence of calculus, neoplasm, or biliary duct compression could be identified. As a result of this finding, a diagnosis of "alcoholic hepatitis" was considered most likely, the surgery was cancelled, and plans for conservative management were made. Over the following three weeks, the patient progressively improved with the laboratory studies returning to normal prior to discharge from the hospital.

Case 2 – A 66-year-old white female entered the hospital with a history of fatigue, malaise, nausea, anorexia, and intermittent fever of approximately three weeks' duration. Three days prior to admission she noted the onset of dark urine and light colored stools which was soon followed by the appearance of jaundice. She denied itching, pain, weight loss, and had no history of drug ingestion.

Physical examination revealed an icteric, alert, and oriented patient. Abdominal examination revealed the presence of mild right upper quadrant tenderness; there was no hepatomegally. The remainder of the examination was unremarkable.

Laboratory studies revealed the following values: hematocrit, 41%; WBC, 9,600 with a normal differential; total protein, 8.2 Gm/100ml (albumin 4.0 Gm/100ml and globulin 4.2 Gm/100ml); sedimentation rate, 68mm per hour; serum bilirubin, 6.2 mgms% (direct, 3.9 mgms%) which rose to 22.8 mgms% (direct, 12.8 mgms%); alkaline phosphatase, 310 I.U./L which rose to 770 I.U./L; SGOT, 105 I.U./L; serum cholesterol, 237 mgms% which rose to 543 mgms%; FBS, BUN, creatinine, urine analysis, prothrombin time, amylase, lipase, cephalin flocculation, thymol turbidity, and serology were all normal, x-rays of the chest, abdomen, upper GI series, and barium enema were all normal.

On admission to the hospital, a diagnosis of viral hepatitis had been made and conservative management planned. Although laboratory studies favored a diagnosis of obstructive jaundice, the differential between extrahepatic obstruction and hepatocellular disease with intrahepatic cholestasis could not be made.

After four weeks of hospitalization and steadily rising liver function tests, an exploratory laporatomy preceded by percutaneous transhepatic cholangiography was planned. Accordingly, the patient was taken to the Radiology Department where a PTC was carried out under local anesthesia. This study revealed the presence of a dilated common bile duct and intrahepatic biliary radicles. The common bile duct was completely obstructed just beyond the cystic duct entry and its configuration suggested a neoplastic etiology.

Following the procedure, the patient was taken to the operating room where an exploration was carried out. On opening the abdomen, the gallbladder was found to be grossly distorted. There was no bile and a minimal amount of blood in the peritoneal cavity. A 6 cm hard, firm mass could be palpated in the head of the pancreas which protruded above the surface of the pancreas and against the common bile duct. An adjacent lymph node was submitted for frozen section and revealed metastatic carcinoma. A cholecystojejunostomy was carried out and the abdomen closed. Final pathologic sections revealed an adenocarcinoma of the pancreas. The patient did well following surgery and was discharged on the seventh postoperative day.

Fig. 4 – Case 4. Marked dilatation of the common bile duct and intrahepatic biliary radicles with complete obstruction of the common bile duct.

Case 3 – A 77-year-old white male entered the hospital with a five-day history of epigastric discomfort, dark urine, light colored stools, and followed by the onset of jaundice. He reported a loss of appetite and feeling poorly during the month prior to admission, but denied symptoms of nausea, vomiting, or itching.

The physical examination on admission revealed an alert, oriented, well nourished patient in no distress. Marked icterus of the sclerae and skin was evident. The abdomen revealed mild tenderness in the epigastrium with a sensation of fullness in the same region. The remainder of the physical examination was unremarkable.

Laboratory studies revealed the following values: hematocrit 35%; WBC, 7,900 with 71% segmented neutrophiles; fasting blood sugar, 137 mgms%; alkaline phosphatase 560 I.U./L; SGOT, 185 I.U./L; SGPT, 220 I.U./L; serum bilirubin, 22.4 mgms% (11.8 mgms% direct); BUN, prothrombin time, calcium, phosphorus, amylase, lipase, serum electrophoresis, cephalin flocculation, thymol turbidity, stool for occult blood, and serum electrolytes were within normal limits. Chest x-ray, upper GI series including hypotonic duodenography, and barium enema were normal.

With a diagnosis of obstructive jaundice, the patient was taken to the Radiology Department where, under local anesthesia, percutaneous transhepatic cholangiography was carried out. This study revealed a markedly dilated common bile duct and intraheptic biliary tree with obstruction to the common duct 2 cm below the entry of the cystic duct. The irregularity of the obstructing lesion suggested a neoplastic etiology rather than a retained calculus.

Immediately following this procedure, the patient was taken to the operating room where an exploratory laparotomy was carried out. On opening the abdomen, there was no evidence of bleeding or leakage of bile from the preceding cholangiogram. A dilated gallbadder without stones was found in association with a dilated common bile duct. A mass in the head of the pancreas which surrounded the common bile duct was palpated; frozen section of an adjacent node revealed adenocarcinoma. Common duct exploration revealed complete occlusion of the duct lumen. Accordingly, a choledochoduodenostomy was carried out and the operative procedure terminated.

Fig. 5 – Case 5. Moderately dilated common bile duct and intrahepatic biliary tree. Note the presence of a radiolucent defect above the Ampulla of Vater.

Case 4 – A 50-year-old white female was admitted to the hospital for evaluation of jaundice of approximately three months' duration. Eight months prior to admission the patient underwent cholecystectomy at which time carcinoma of the gallbladder was found. Three months prior to admission the patient developed nausea and vomiting, and noted weight loss, dark urine, and pale stools. A diagnosis of metastatic disease to the liver originating from the carcinoma of the gallbladder was made and the patient treated with a course of 5-Flurouracil®. The patient continued to do poorly and one week prior to admission developed intense pruritus. The possibility of extrahepatic biliary obstruction amenable to surgery rather than metastatic disease to the liver was considered and the patient admitted for evaluation.

Physical examination on admission revealed a markedly jaundiced, alert and oriented patient in no distress. Abdominal examination found an enlarged liver measuring 8 cm below the right costal margin without definite nodularity. The remainder of the examination was unremarkable.

Laboratory studies revealed the following results: hematocrit, 39%; WBC, 7,500 with 89% segmented neutrophiles; alkaline phosphatase, 250 I.U./L; SGOT, 35 I.U./L; SPGT, 17 I.U./L; serum bilirubin, 25.5 mgms% (14.5 mgms% direct); serum protein, 6.8 Gm/100ml (albumin 3.1 Gm/100ml); BUN, FBS, amylase, lipase, calcium, phosphorus, serum electrolytes, and prothrombin time were normal. A chest x-ray was normal.

On the seventh hospital day, the patient was taken to the Radiology Department where under local anesthesia, a percutaneous transhepatic cholangiogram was carried out. The study revealed marked dilatation of the intrahepatic biliary radicles and complete obstruction of the common bile duct 2.5 cm distal to its origin. As a result of these findings, the patient was taken to the operating room where on exploration the region of the porta hepatis was found to be significantly infiltrated by tumor which resulted in complete obstruction of the common bile duct. The liver was noted to have a moderate number of metastatic nodules on its surface. A posterior gastroenterostomy and Roux-en-Y hepatojejunostomy was performed. Biopsy of

Fig. 6 – Case 5. In this closer view of the radiolucent defect, contrast material can be seen to flow around the calculus confirming incomplete extrahepatic obstruction.

the tumor mass revealed adenocarcinoma consistent with gallbladder origin. The postoperative course was uneventful, the jaundice subsided, and the patient was discharged home on the 27th hospital day.

Case 5 – A 35-year-old white female was well until one week prior to admission when she experienced moderately severe right upper quadrant pain with radiation to the right subscapular region. The pain was constant in nature and recurred intermittently over the next several days. During this time, she noted that her urine became dark, her stools light yellow, and shortly thereafter observed seleral and cutaneous jaundice.

Physical examination revealed a jaundiced but alert patient in no acute distress. The abdomen was soft with mild tenderness in the right upper quadrant. The liver was not enlarged, and no masses were palpated. The remainder of the examination was unremarkable.

Laboratory studies revealed the following: serum bilirubin, 6.1 mgms% (4.3 mgms% direct); alkaline phosphatase 90 I.U./L; SGOT, 76 I.U./L; SGPT, 94 I.U./L; sedimentation rate, 40 mm per hour; urine urobilinogen, 1 Ehrlich unit; CBC, BUN, blood sugar, prothrombin time, serum proteins, cephalin flocculation, and serology were normal. Serial liver function tests revealed a gradual rise in serum bilirubin and all enzymes.

Because the clinical course and laboratory studies could not differentiate between viral hepatitis with intrahepatic cholestasis and partial or incomplete extrahepatic biliary obstruction, a percutaneous transhepatic cholangiogram was performed to aid in clarifying the diagnosis. The study revealed the presence of a moderately dilated common bile duct and intrahepatic biliary tree. Within the common duct, a radiolucent defect resembling a calculus was identified with small amounts of contrast material passing by the obstruction on either side. A diagnosis of partial common bile duct obstruction secondary to cholelithiasis was made and the patient taken to surgery. At the time of laparotomy, exploration of the common duct revealed multiple calculi in addition to the large stone demonstrated preoperatively by cholangiography. Cholecystectomy was carried out and a subsequent T-tube cholangiogram revealed the bile ducts to be free of calculi. Postoperatively the patient did well and was discharged home on the twelfth day following surgery.

Discussion

The value of percutaneous transhepatic cholangiography as an aid in the evaluation and elucidation of obstructive jaundice has been demonstrated by these examples. In each case, the procedure played a major role in the diagnostic evaluation of the patient. In Case 1, PTC differentiated intrahepatic from extrahepatic biliary obstruction and unnecessary surgery was thereby avoided. Case 2 represents a patient who was thought to have viral hepatitis with a prolonged cholestatic phase, but in whom PTC demonstrated complete occlusion of the common bile duct and confirmed the need for surgical intervention. In Case 3, the procedure correctly demonstrated the exact site of the extrahepatic obstruction as well as correctly identifying neoplastic disease as the cause. In Case 4, this diagnostic technique identified the presence of extrahepatic obstruction in a patient known to have metastatic disease to the liver and thereby aided in obtaining palliation for the patient through surgical bypass of the obstruction. Case 5 is an example where PTC provided the means to differentiate viral hepatitis in the cholestatic phase from partial or incomplete extrahepatic biliary obstruction. These cases represent examples of common clinical situations where a diagnostic dilemma often exists, and in which the technique of percutaneous transhepatic cholangiography may be instrumental in the resolution of the problem.

The first successful percutaneous transhepatic cholangiogram was performed by Huard in Indochina[12] in 1937. He reported the use of this procedure in the visualization of parasites of the biliary tree and in patients with apparent obstruction. In 1952, Carter and Saypol[4] again brought this technique to the attention of others by reporting the first successful procedure in the English literature. Remolar[13] in 1956 suggested a more widespread use of this procedure extending to the community hospital and noted the relative ease with which the procedure could be performed and with a minimum of equipment, time, and personnel. In the same year, Kidd[14] established the indications for its use including several infrequently considered areas such as measuring the pressure of bile in the biliary system in cases of suspected spasm of the Sphincter of Oddi, and to investigate apparent biliary symptoms after cholecystectomy. Shaldon[10] in 1962 modified the technique by introducing a polyethylene catheter around the needle which could be left in place after removal of the needle. This modification provided greater safety during the procedure and also provided a ready means of decompression of the biliary system if surgical relief of the obstruction was not possible in those patients who represented an extremely poor surgical risk.

The indications for the use of percutaneous transhepatic cholangiography are as follows: (1) to differentiate between intrahepatic and extrahepatic biliary obstruction; (2) to determine and locate the site and cause of the obstruction in obstructive jaundice of the extrahepatic type; and (3) the postoperative evalua-

tion of the common duct if the duct was injured, or thought to be injured, at the time of surgery. The first indication is probably the most important one as this procedure may be instrumental in determining the necessity for surgery, or conversely, the advisability of conservative management. If a dilated biliary tree is found, the need for surgical intervention is confirmed; however, if a normal biliary system is noted a biopsy may be taken to aid in the diagnosis, and unnecessary surgery averted. Evans[6] reported in the *Journal of Radiology* in 1964 that the use of percutaneous transhepatic cholangiography triples the number of positive preoperative diagnoses of carcinoma of the pancreas as compared to the upper gastrointestinal series and almost doubles the diagnostic accuracy in carcinoma of the Ampulla of Vater. Importantly, the feature common to all the indications and the features of this technique over other methods of cholangiography is the fact that it can circumvent the inability of the liver to excrete iodinated compounds when even a minimal degree of hyperbilirubinemia is present.

Approximately 75-80% of attempts are successful[3,6] in that the biliary tree may be entered, radiographic media injected, the ductal system visualized, and a cause of the obstruction identified. If, on the other hand, the bile ducts cannot be entered and, therefore, presumably dilatation does not exist, a longer period of medical therapy is warranted and unnecessary surgery may be avoided. Liver biopsy may then be performed during this interval to aid in establishing the correct diagnosis. Mulero and Carvalho[2] have stated that the degree of dilatation of the ducts depends more upon the duration of jaundice rather than upon the depth of jaundice; this fact must be taken into consideration when interpreting the significance of a failure to enter a bile duct during the course of this procedure.

Several studies[15,16] have shown that 40-50% of patients with partial biliary obstruction have gram-negative organisms and occasionally *Staphylococcus aureus* in their bile, not necessarily associated with fever and chills. Because of the potential danger of producing septicemia during the course of the procedure, it is recommended that antibiotics be administered prior to and after cholangiography. (See Method). In addition, some of the aspirated bile should be sent for routine bacteriologic cultures.

In a small percentage of cases, a positive cytology may be obtained from the bile of patients with metastatic disease or primary malignancy of the biliary tree.[2] Several slides may be made from the aspirated bile and sent for cytological examination to aid in the diagnosis.

A positive percutaneous transhepatic cholangiogram with dilatation of the biliary tree and the demonstration of extrahepatic obstruction may be seen with such examples as calculi of the common bile duct or hepatic ducts, carcinoma of the pancreas, or carcinoma of the Ampulla of Vater. A negative cholangiogram, defined by either the failure to enter a bile duct or by the demonstration of a normal biliary tree, may be seen in instances of drug induced cholestasis, viral hepatitis, hepatoma, metastatic carcinoma, or biliary cirrhosis. Rarely, false positive cholangiograms have occurred when air bubbles have been introduced at the time of injection of the dye simulating calculi.[11] A false negative test may theoretically occur when there is inspissated bile from long standing extrahepatic obstruction.[11] (False negative in the sense that failure to enter and visualize the biliary tree leads to a diagnosis of intrahepatic obstruction when in fact the cause is extrahepatic.) Fortunately, however, the incidence of false positive and false negative cholangiograms is extremely small.

Complications, although unusual, have been reported. Transient pain occurs following the procedure in slightly over one-half of patients[2] but is easily controlled by analgesics. Bile peritonitis, although often feared, is quite unusual. Zinberg[11] reviewed a series of 423 percutaneous transhepatic cholangiograms in which the incidence was 3%, and bile leakage noted at the time of laporatomy, but without clinical signs of peritonitis, found in an additional 1.7%. Puncture of the gallbladder has occurred but has been without consequence.[17] Bleeding has been reported in slightly more than 1% of cases except when carried out in those patients in whom the clotting and coagulation studies were abnormal prior to the procedure.[6] Tension pneumothorax,[18] hematobilia,[18] and blood clots in the common duct causing further aggravation of the obstruction[3] have been reported. Puncture of the colon or small bowel may occur,[2] but has not been reported to cause symptoms or complications. Additionally, septicemia has been noted[15,16] because such a high percentage of these patients have infected bile as a result of biliary obstruction.

Summary

The technique of percutaneous transhepatic cholangiography as an aid in the differentiation of extrahepatic and intrahepatic biliary obstruction as well as the demonstration of the nature and location of an extrahepatic obstructive lesion is presented. Five cases are described in which this procedure was of value in the diagnosis and management of each patient. The method and procedure for employing this technique is described, and a discussion of its expected merits as well as possible complications is included.

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William L. MacVane, Jr., M.D., 211 State St., Portland
Maine Hospital Association members –
Mr. Lee W. Pridgen, Jr., Adm., Augusta Gen. Hosp., Augusta
Richard W. Britt, M.D., Adm., Blue Hill Mem. Hosp., Blue Hill

Continued on Page 268

Maine Heart Association Notes

20 Winter Street, Augusta, Maine

General Highlights of Cardiac Auscultation

JOSEPH K. PERLOFF, M.D.*

The practical use of cardiac auscultation requires an understanding of certain elementary principles. First, auscultatory events must be *heard* before they can be interpreted; accordingly, the technicalities and techniques of auscultation are paramount. Second, recognition of the various heart sounds, especially the first and second sounds, defines systole and diastole and establishes the timing of the different phases of the cardiac cycle. Third, the timing of murmurs can readily be accomplished once the phases of the cardiac cycle are defined. The following remarks will touch on each of these three principles.

Technicalities and Techniques – The chain of success in this area consists of a number of links. The *instrument* of auscultation is the stethoscope that was introduced by Laennec in 1819. The ideal stethoscope is yet to be devised but good instruments are available and certain guidelines are useful in their selection. Both a bell and a diaphragm are necessary, the former for the low frequency ranges and the latter for the high. Connecting tubing should be relatively firm and single; double tubes are acoustically less efficient and cause extraneous noise when they touch or rub together. The overall length of the entire stethoscope should be about 22 inches. The binaural ear pieces should be relatively large so that they occlude the external auditory canals and do not uncomfortably enter them. Finally, all connections must be airtight in order to avoid loss of sound by leakage.

The next link in the chain is the sensing device, i.e. the human ear which can be trained to sense the broad range of frequencies eminating from the heart and blood vessels. It is encouraging to know that the ear is more efficient than the phonocardiogram in recognizing high frequencies such as the soft murmur of aortic incompetence. The ears are all important since even the best stethoscopes do *not* amplify sound but merely transmit it to the ears with relatively little loss. Perhaps the most important link in the chain is the interval between the stethoscopic ear pieces, namely, the human brain. The brain interprets what is heard, and in order to do so effectively it must be programmed by years of experience. Once these technical links – the instrument, the sensing device, the interpreter and the programming – are forged, we can turn attention to the auscultatory technique itself.

Auscultation should be conducted in a quiet examining room that is free of ambient noise and that has a temperature so regulated as to avoid shivering. The patient must be relaxed and comfortable and the examiner unhurried. Various postures should be employed such as supine, prone, left lateral decubitus, sitting, leaning forward, standing, or squatting. Respiratory patterns should also be appropriately selected including quiet or arrested breathing for routine auscultation, full held expiration for the soft murmur of aortic incompetence, or normal or exaggerated respiratory excursions for the behaviour of the second heart sound or for certain right-sided events. Physical and pharmacologic interventions are useful and include coughing, effort, squatting, isometric tension (squeezing the clinched fists), and certain vasoactive drugs especially amyl nitrite and pressor agents. When the bell of the stethoscope is applied with varying degrees of pressure, a relatively broad range of frequencies can be elicited. When the bell is touched lightly to the skin, low frequencies are heard (soft third heart sound); when high frequencies are paramount, firm pressure with the diaphragm is required. Palpation should precede auscultation so that the stethoscope can be placed precisely at the most appropriate precordial sites. Finally, auscultation should not be confined to the procordium but should include the right chest, axillae, back, neck, flanks, abdomen, groins, and at times the eyeballs and skull.

The Heart Sounds – The normal heart sounds define the phases of the cardiac cycle and serve as standards by which abnormal heart sounds can be judged. The first heart sound is best assessed at the apex or lower left sternal edge and is either single or closely split. Splitting is usually confined to the lower sternal edge and is normally not heard at the base. Although analysis of the first heart sound provides helpful information, analysis of the *second* heart sound is far more useful and has been called the key to auscultation of the heart. Proper interpretation of the second sound assumes an awareness of its location, splitting, and intensity. In the second left intercostal space there are two components, aortic and pulmonic, which are synchronous (or nearly so) during expiration and split during inspiration. A judgment regarding the intensity of pulmonary

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Prepared by the Maine Heart Association for this Journal.

valve closure requires comparison with aortic closure when *both* sounds are heard simultaneously during inspiration. The comparative softness of the pulmonary closure sound is held responsible for its localization in the vicinity of the second left intercostal space, and the relative loudness of aortic closure accounts for its audibility at all areas. It should clearly be stated that A_2 refers to *aortic* valve closure and P_2 to *pulmonary* valve closure. A_2 and P_2 do *not* refer to the second heart sound in the "aortic" vs. the "pulmonary" area; such use implies a complete misunderstanding of the origin of the two components of the second sound. Similarly, P_2 by definition is a single sound caused by pulmonary valve closure, so the expression "split P_2" is a misnomer that should be abandoned.

The third and fourth heart sounds are best understood in relation to the two diastolic phases of ventricular filling. These sounds originate *within* the recipient ventricle, the third sound during the middiastolic filling phase and the fourth sound during the presystolic filling phase. Accordingly, a fourth heart sound implies sinus rhythm. Both sounds are low frequency events that are most readily heard with light touch of the stethoscope bell.

The foregoing heart sounds – first, second, third, and fourth – can either be normal or abnormal. The following sounds are, foi all practical purposes, abnormal events.

Opening snaps characteristically originate in the mitral valve usually because of stenosis. The snap is relatively high frequency, is heard not only at the apex but also at the sternal edge and base, and is best elicited with the stethoscopic diaphragm or firm pressure with the bell. Since the mitral valve must open before the ventricle can fill, the timing of the opening snap necessarily precedes the timing of the third heart sound.

Ejection sounds are high pitched, clicking early systolic events that originate in either the left heart (aortic valve or dilated ascending aorta) or right heart (pulmonic valve or dilated pulmonary trunk). These sounds tend to be heard at the *base* of the heart and should not be mistaken for split first heart sounds. The aortic ejection sound is well-heard at both the base and apex and with rare exception does not vary with respiration; the pulmonic ejection sound is well-heard in the second left intercostal space and often varies characteristically with respiration, getting selectively softer with inspiration and louder with expiration.

Systolic clicks must be distinguished from ejection sounds. The clicks are similar to ejection sounds in frequency but not in timing or chest wall location. Clicks generally originate in redundant mitral chordae tendineae; they are single or multiple, maximal at the apex, and begin in mid to late systole.

Cardiac Murmurs – A cardiovascular murmur is a relatively prolonged series of auditory vibrations characterized according to intensity (loudness), frequency (pitch), configuration (shape), quality, duration, direction of radiation and timing in the cardiac cycle. The timing of murmurs is particularly important since it serves as a basis for classification. Systolic murmurs are classified according to their time of onset and termination as midsystolic, holosystolic, early systolic, or late systolic. A midsystolic murmur begins after the first heart sound and ends before the second sound (aortic stenosis). A holosystolic murmur begins with the first heart sound, occupies all of systole, and ends with the second heart sound (classic mitral incompetence). Early systolic murmurs begin with the first heart sound, diminish in a decrescendo fashion, and end at or before midsystole (very small ventricular septal defect with early systolic shunt). Late systolic murmurs begin in mid to late systole and end with the second heart sound (mitral incompetence with late systolic regurgitation). Finally, *extracardiac systolic arterial murmurs* originate in either systemic or pulmonary arteries. The existence of such murmurs emphasizes the importance of careful auscultation at nonprecordial sites.

Diastolic murmurs are classified according to their time of *onset* as early diastolic, middiastolic, or late diastolic (presystolic). An early diastolic murmur begins with the second heart sound (aortic incompetence). A middiastolic murmur begins at a clear interval after the second heart sound (mitral stenosis with atrial fibrillation). A late diastolic murmur or presystolic murmur begins in the period immediately before the first heart sound (mitral stenosis with sinus rhythm).

The term "continuous" is best applied to murmurs that begin in systole and continue without interruption through the time of the second heart sound into all or part of diastole. Persistence of murmurs throughout the cardiac cycle is therefore not a requirement. Accordingly, a murmur that proceeds into diastole without stopping at the second heart sound is considered continuous whether or not it finishes before the next first heart sound. Continuous murmurs can be due to aortopulmonary communications (patent ductus), arteriovenous connections (systemic arteriovenous fistulas), or can be purely arterial (arterial constriction), or purely venous (venous hum).

Summary

There are few areas of clinical cardiology that auscultation does not animate. This paper has reviewed three areas relevant to this topic: 1) the technicalities and techniques of auscultation, 2) the heart sounds), and 3) cardiovascular murmurs. Skill in auscultation remains a hallmark of the good clinician and it is understandable why this is so.

Necrologies

Nathaniel Mills, M.D.

1885-1970

Dr. Nathaniel Mills, 85, of Wolfeboro, New Hampshire and formerly a resident of Harrison, Maine, died on September 30 following a long illness.

He was born in Mt. Vernon, New York on September 22, 1885, son of Judge and Mrs. Isaac Newton Mills.

Dr. Mills was graduated from Williston Academy in Easthampton, Massachusetts, Williams College in 1908 and received his medical degree from Johns Hopkins University School of Medicine in 1912. He practiced medicine in Mt. Vernon, New York from 1914 to 1943. In 1943, Dr. Mills located in Bath, Maine where he served as orthopedic surgeon for the Bath Iron Works. Dr. Mills practiced in Pownal from 1946 to 1952 and in Harrison for approximately ten years before moving to Wolfeboro, New Hampshire.

He was an honorary member of the Oxford County Medical Society and the Maine Medical Association, having received a 50-year pin in 1962 and a 55-year pin in 1967. Dr. Mills was also a member of the American Medical Association, a life member of the Williams College and Johns Hopkins Alumni Associations, and was on the teaching staff of Columbia University for many years.

Surviving are his widow, the former Edith Williams and a nephew.

Louis C. Lesieur, M.D.

1913-1970

Dr. Louis C. Lesieur, 57, who practiced in the Biddeford-Saco area since 1940, died on October 26 after a long illness.

He was born in Rumford, Maine on May 24, 1913, son of Dr. Louis O. and Marie B. Lesieur.

Dr. Lesieur attended the School of Foreign Service at Georgetown University and then transferred to the University of Maine pre-medical course. He received his medical degree from the Georgetown University School of Medicine in 1938. Dr. Lesieur served an internship and residency at the Misericordia Hospital in New York City from 1938 to 1940 and then located in Saco.

From 1942 to 1946, Dr. Lesieur served with the U.S. Army Air Force as a flight surgeon. He was graduated from the School of Aviation Medicine at Randolph Field in Texas, and studied extensively in the field of aviation medicine and surgery, neuropsychiatry and aviation physiology. He spent 18 months in India in charge of an Air Force hostel for flight surgeons flying the Hump into China. At the time of his discharge in 1946, Dr. Lesieur held the rank of Colonel.

After resuming practice in Saco as an internist, Dr. Lesieur completed many courses in medical use of radioactivity and was licensed by the Atomic Energy Commission to teach radioactivity and electronic physics.

Dr. Lesieur was a member of the York County Medical Society, the Maine Medical Association and the American Medical Association.

Surviving are five sisters, Mrs. Arthur Roberge of Biddeford, Miss Marguerite Lesieur, Mrs. Gabrielle Howell, R.N. and Mrs. Frederick Patterson, R.N., all of Saco, and Mrs. Hallis Little of Billerica, Massachusetts; two brothers, Maurice A. Lesieur of Biddeford and Paul E. Lesieur of Saco; several cousins, nieces and nephews.

County Society Notes

PENOBSCOT

A regular meeting of the Penobscot County Medical Society was held on April 21, 1970 at the Tarratine Club in Bangor, Maine with the President, Dr. Edward L. Curran, presiding. A quorum was present.

The minutes of the previous meeting were approved as read.

The Committee Report concerning the difficulty between the physicians in Lincoln, Maine and Mr. William Carney's office in Augusta was read by Dr. Edward B. Babcock. It was recommended that a copy of the report be forwarded to the State Medical Association.

Thereafter, the reports of the subcommittees of the M.M.A. Priority Committee were discussed. A copy of the reports had been distributed during the week prior to the meeting. The following consensus was brought forth:

1. Distribution of the Health Services Subcommittee Report. Many aspects of the report in general could not be concurred with by the Society. Dr. Edward C. Porter recommended the concept of establishing Health Service Centers, possibly associated with hospitals by geographic areas within the State. This concept was passed. Dr. Richard A. Gaillard had recommended a tabling of the above motion with referral for a subcommittee. This was not passed. In that he had not received a copy of the subcommittee reports until shortly prior to the meeting, he felt that it was difficult to adequately discuss the reports prior to having more time for consideration.
2. Ethics and Discipline Subcommittee Report.
   Dr. Robert O. Kellogg motioned that each County Executive Committee act as a Board of Censors for ethics and discipline. This was passed.
3. Health Financing Subcommittee Report.
   The report in general was approved. There was some disagreement with Item #4 at the bottom of Page 2 regarding duplication of effort and facilities, feeling that some competition at times is beneficial. A question also was raised regarding the last sentence in Paragraph 2 on Page 2 regarding fixed salary and associated laziness.
4. Health Manpower and Recruitment Subcommittee Report.
   The report was approved.
5. Comprehensive Health Planning Subcommittee Report.
   It was motioned the report be accepted other than Item

#5. Seven were for and eleven against the motion. Discussion regarding the merits of consolidation versus competition in some aspects of medicine followed.

6. M.M.A. Organization Subcommittee Report.
The report was approved, particularly agreeing with the need for reorganization into larger groups, although not particularly as there proposed.
7. Medicine and Law Including Malpractice Subcommittee Report.
No further specific recommendations were made, recognizing the need for legal evaluation.
8. Nursing Needs Subcommittee Report.
It was concurred that further evaluation was apparently needed.
9. Osteopathic Subcommittee Report.
Dr. Robert P. Andrews motioned that the report be accepted with the word "could" being substituted for the word "should" in the second line of paragraph 3 on Page 2. Eight voted for and nine against the motion. Dr. George W. Wood, III recommended the report be accepted for information, with this being passed.
10. Paramedical Personnel Subcommittee Report.
Report noted.
11. Peer Review Subcommittee Report.
Dr. Hadley Parrot opposed having the problem-oriented record concept as the only concept for review. Dr. Thornton W. Merriam, Jr. concurred with having a peer review and suggested that first there should be further evaluation of the means of the review. It was concurred that personnel should function outside their practice areas.
12. Emergency Services Subcommittee Report.
Report noted.

It was motioned that delegates be instructed to advise of Penobscot County's acceptance of increased yearly State dues to $85.00. This was approved.

LEWIS E. PHILLIPS, M.D., *Secretary*

CUMBERLAND

The 354th meeting of the Cumberland County Medical Society was held at the Purpoodock Country Club in Cape Elizabeth, Maine on September 17, 1970. The meeting was preceded by an afternoon of golf and softball with free refreshments provided by the Cumberland County Medical Society. A dinner catered by Mrs. Mildred Clough was served sixty-five members and guests, a disappointing turnout. It was felt in the future that perhaps better advertisement and prior notice would result in better attendance, if this is to become a yearly affair.

The business meeting was called to order at 8:00 p.m. Five members were accepted into membership in the Cumberland County Medical Society. Those receiving their second reading, therefore, having been approved by the committee were: Drs. Frederick G. Delaney, John C. Serrage, George P. Lord and Joseph H. Edgar, Jr. Dr. Nicholas Fish was accepted as a transfer member on a letter of recommendation from York County and upon application of Dr. Fish for transfer. Members receiving a first reading of their membership applications were: Drs. Takanori Kimura, Roland G. Ware, Jr., William H. Austin and William Hall. These first readings of application for membership were set aside to be voted upon at the next meeting of the membership after review by the committee.

There being no other business of major note to come before the Society, the meeting was adjourned by Dr. George F. Sager.

The 355th meeting of the Cumberland County Medical Society was held on October 15, 1970 at the Stage Coach Restaurant in South Portland, Maine. A good crowd of seventy-seven members and guests was present. After a social hour and an excellent dinner of Prime Ribs of Beef, the business meeting was called to order by the President, Dr. George F. Sager.

The minutes of the last meeting were read and approved after a correction in wording had been made as suggested by Dr. Howard P. Sawyer, Jr.

A letter from the Maine Association of Medical Assistants was read by the Secretary. This organization desires to set up a medical registry which would list the qualifications of applicants whose names would be forwarded to perspective employers for consideration. The Cumberland County Medical Society was in agreement that this was a good idea; and it was moved, seconded, and voted by the Society to support this organization with a check for $100.00 to assist the Maine Association of Medical Assistants in setting up the medical registry.

A letter from Scarborough Downs was read by President Sager. Scarborough Downs was notifying the Cumberland County Medical Society that a position for a physician existed at their track. Anyone who is interested in this job and wishes further details should contact the Secretary of the Cumberland County Medical Society.

President Sager then introduced members of the Society who have been taken in during the last two meetings and who were in attendance at the meeting of October 15th. These included Drs. Robert P. Timothy, John T. Dinan, Jr., William H. Leschey, Douglass W. Walker and George P. Lord.

President Sager then called on our representative, Dr. Robert F. Ficker. Dr. Ficker brought us up to date on the actions of the Council with regard to drugs and the drug situation, the S.T.O.P. Committee, the area of redistribution, and announced that the Osteopath-M.D. Board of Registration had taken one more step forward toward reality.

The applications of Drs. William Hall, Takanori Kimura, Roland G. Ware, Jr. and William H. Austin were read for the second time. These applications were approved by the Cumberland County Medical Society and these men were voted into membership in the Society.

The applications for membership to the Cumberland County Medical Society of Drs. Kenneth Gluck and Robert Milsovic were read for the first time.

Dr. Sager read the resolution on the death of Dr. Robert A. Bearor.

The Cumberland County Medical Society then took up special memberships. The Society voted into Honorary Membership Dr. Leon Babalian, graduate of the School of Medicine of Paris in 1921, and Dr. Edward Blumberg, graduate of the University of Leipzig, Saxony in 1921. The Society members also voted into Affiliate Membership Drs. Norman E. Dyhrberg, Roderick L. Huntress, Doris M. Sidwell-Thompson, John B. Titherington and John V. Ward.

There then followed a discussion of dues. It was agreed, moved, seconded, and voted to increase the dues of the Cumberland County Medical Society from $25.00 to $30.00. The dues to be collected by the Secretary in Brunswick and prorated as usual.

The Cumberland County Medical Society acknowledges receipt of pictures of the Cumberland County Medical Society membership of 1939. These are to be held by the Cumberland County Medical Society. However, the Society has decided to give these pictures to the Maine Medical Center Library for their historical value. The Librarian has been notified and was delighted to receive them. They will be on display at the Library.

Dr. Sager then introduced Mr. Stanley Hanson of the Southern Maine Comprehensive Health Association who gave an excellent talk on Comprehensive Health Planning. Mr. Hanson started with the Federal level of medical regional planning and discussed, beginning in 1966, the Federal Government's effort to improve the medical care of the people of the country, including Medicare and Medicaid, regional medical planning, comprehensive health planning, and the Hill-Burton Act. Mr. Hanson then went on to discuss comprehensive health planning

at the State level and finally, Southern Maine Comprehensive Health Planning. He noted that the comprehensive planning at the State level is funded 50% by the Federal Government and the remaining 50%; 1/3 by hospitals; 1/3 by Blue Cross, Union Mutual, and other third party payers; 1/3 by United Community Services and the Diocese. Mr. Hanson went on to discuss the Southern Maine Comprehensive Health Association and its efforts in long-range planning; also, the progress made with relation to radiation therapy, provision of emergency medical service, disaster services, alcoholism, drug abuse, and the mental health systems. Mr. Hanson's talk was followed by a period of lively questions and answers.

The meeting was adjourned by Dr. Sager.

DOUGLAS R. HILL, M.D., *Secretary*

LINCOLN-SAGADAHOC

A meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on September 15, 1970. The meeting was called to order by the President, Arkadij Oceretko, M.D. at 9:05 p.m. The minutes of the previous meeting were read and accepted without revision.

Dr. George W. Bostwick discussed the resignation of Dr. Richard Evans, III in June. After the meeting, the request was changed to Junior Membership. The secretary approved this change during the summer. Dr. Oceretko asked for a motion to approve this change, which was passed unanimously.

Dr. Bostwick then stated that the committee appointed in June to study the Constitution and Bylaws had not met, but would meet for discussions to present proposals in two months or so. He stated that the urgent problem of admission of osteopaths to hospital staffs is a function of hospital staff bylaws and not those of the county medical society.

The report of the Board of Censors was given by Dr. Bostwick, approving the application of Dr. Richard C. Leck, pathologist at Bath Memorial Hospital, who is a transfer from the Rock Island County Medical Society of Illinois.

A letter was read from MEDEX in New Hampshire and not understood. More details will be sought. A letter from the Council of the New England State Medical Societies was read urging upon us a speaker on a Keogh Plan; the consensus of this society was resistant to the urging.

The dues structure and the bank balance of this society were discussed by Dr. Bostwick; Dr. Charles E. Burden moved, and Dr. Frank O. Avantaggio, Jr. seconded, that dues remain at thirty dollars.

Dr. Bostwick introduced Drs. Winifred W. Curtis of Bailey Island and Walter Sieling of Bristol. Dr. Oceretko then gave the meeting over to Dr. Henry A. Hudson, chairman of the Program Committee, who introduced Dr. Robert G. Sommer, who spoke on Psoriasis and Seborrhea.

GEORGE W. BOSTWICK, M.D., *Secretary*

WASHINGTON

The regular meeting of the Washington County Medical Society was held on September 28, 1970 at the Conference Room of the Down East Community Hospital, Machias, Maine with nine members and guests present. Dr. George B. Shaw, President of the Society, presided.

Minutes of the last meeting were read and approved.

Dr. Donald M. Robertson of Milbridge, convenor of a committee to study the foundation and M.I.C. plans with the following members: Drs. George B. Shaw, Machias, Nelson W. Stott, Eastport and Harold G. Sears, Woodland, presented their proposals for a Maternal and Infant Care Program for Washington and Hancock Counties. The proposal is divided into four major parts: 1. Objectives; 2. Operations; 3. Finances and 4. Personnel. These major proposals plus the sub-divisions were discussed step by step by the members present. A motion was made and seconded and the motion passed that we accept this proposal for a Maternal and Infant Care Program for Washington and Hancock Counties. There will be further discussions of the proposal at a combined dinner meeting with the Hancock County Medical Society on October 14, 1970 at 6:30 p.m. at the Red Barn in Milbridge, Maine.

Dr. Stott informed the Society that the Medical Assistance Program run by the Union Mutual Life Insurance Company of Portland, Maine was allowing $.50 a mile one way, after the first three miles, whereas Medicare Health Insurance was allowing $1.00 each mile after the first five miles. A motion was made and seconded and the motion passed that we reaffirm our mileage charges of $1.00 per mile after the first five miles and that the Union Mutual Life Ins. Co. be so informed.

Dr. Shaw read excerpts from the Bennett Amendment 851, Social Security Amendments of 1970, H. R. 17550. This amendment removes quality control of Utilization Review from the hospital staff and places it in the hands of the County Medical Society. It would require the maintenance of profiles and constant review of every patient, every physician, every institution, with a duplication of all physicians' and hospital and medical records. The motion was made and seconded, and the motion passed, that the secretary contact the members of the Senate Finance Committee where the bill is now being read and register our opposition to this particular bill, with copies of our letter to go to Senators Smith and Muskie and our Representative.

Dr. Robert G. MacBride of Lubec, member of the Reorganization Committee of the State Medical Society said that he had no report as yet, since no committee meeting had been held.

Dr. James C. Bates of Eastport, Councilor of the Fifth District, reported on the last Council meeting. He reported the Council discussed the last Maine Medical Association meeting and also reported on visits to the State Mental Hospitals.

KARL V. LARSON, M.D., *Secretary*

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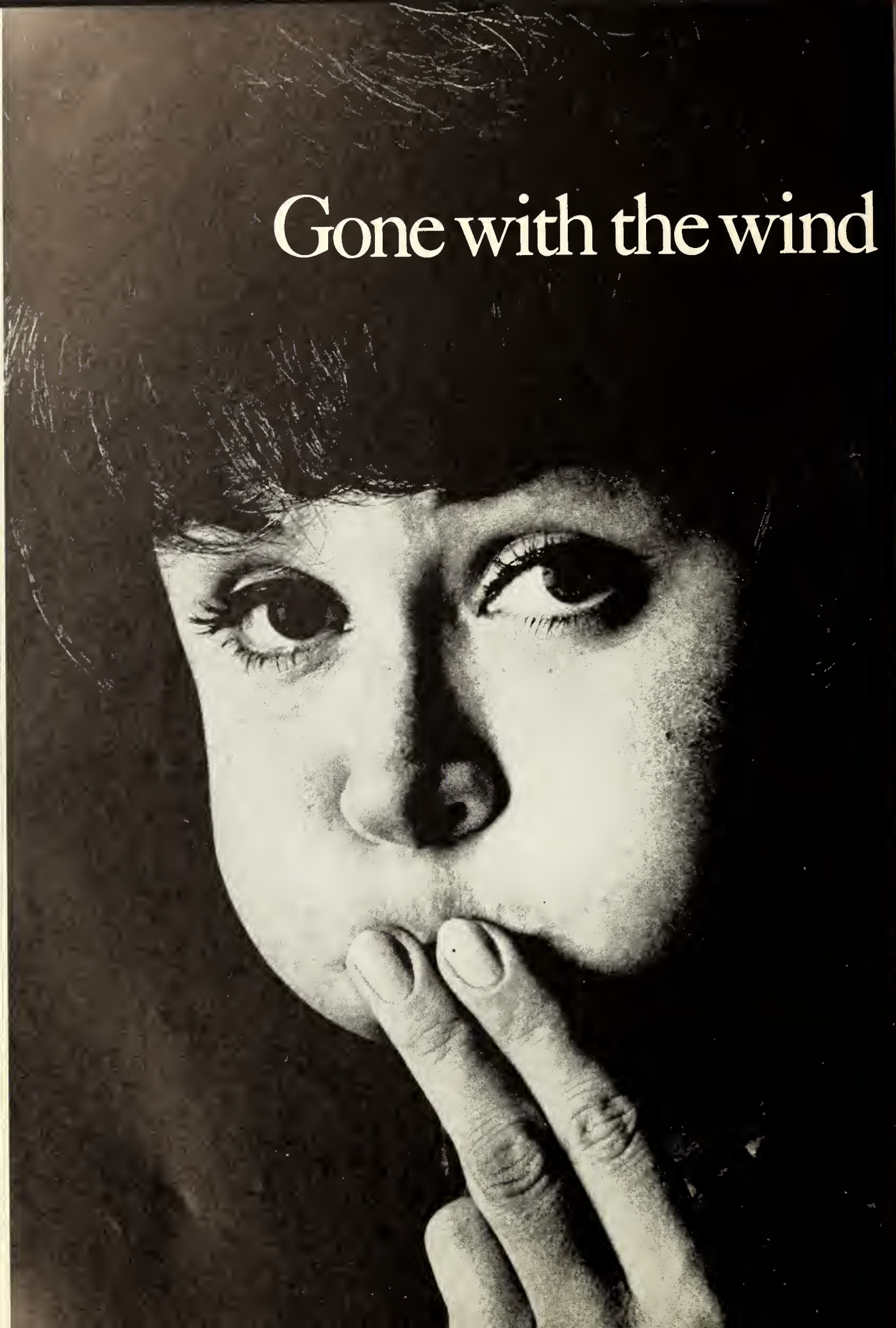

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VOLUME SIXTY-ONE

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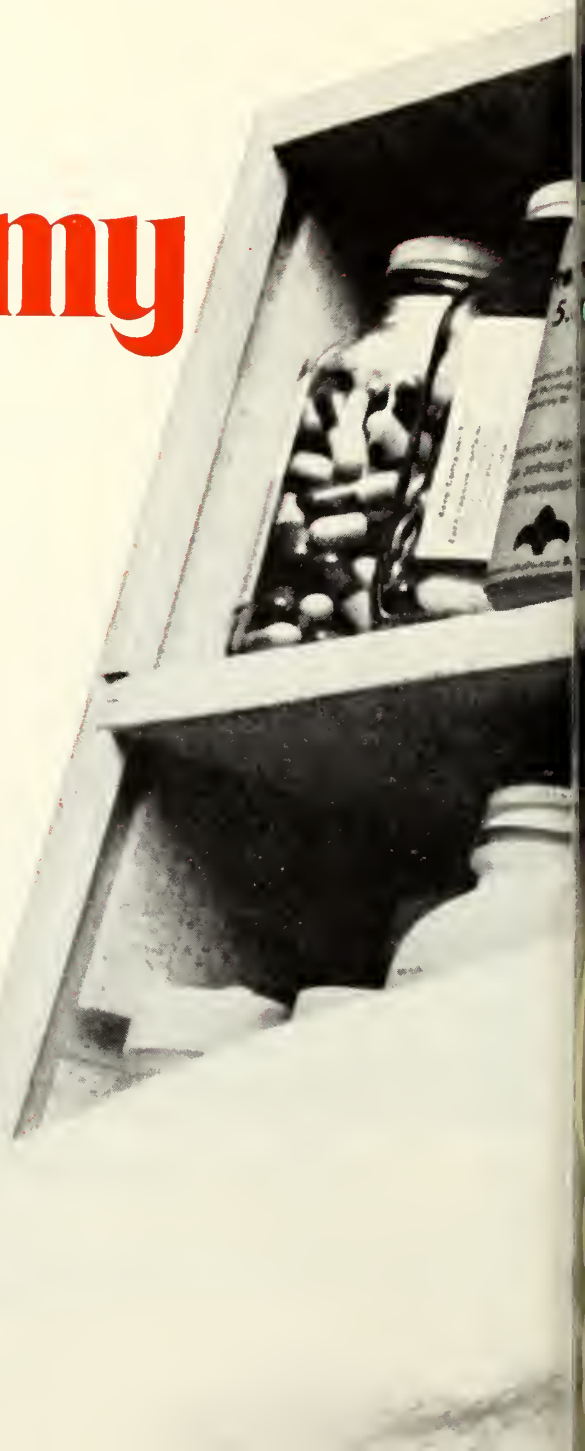

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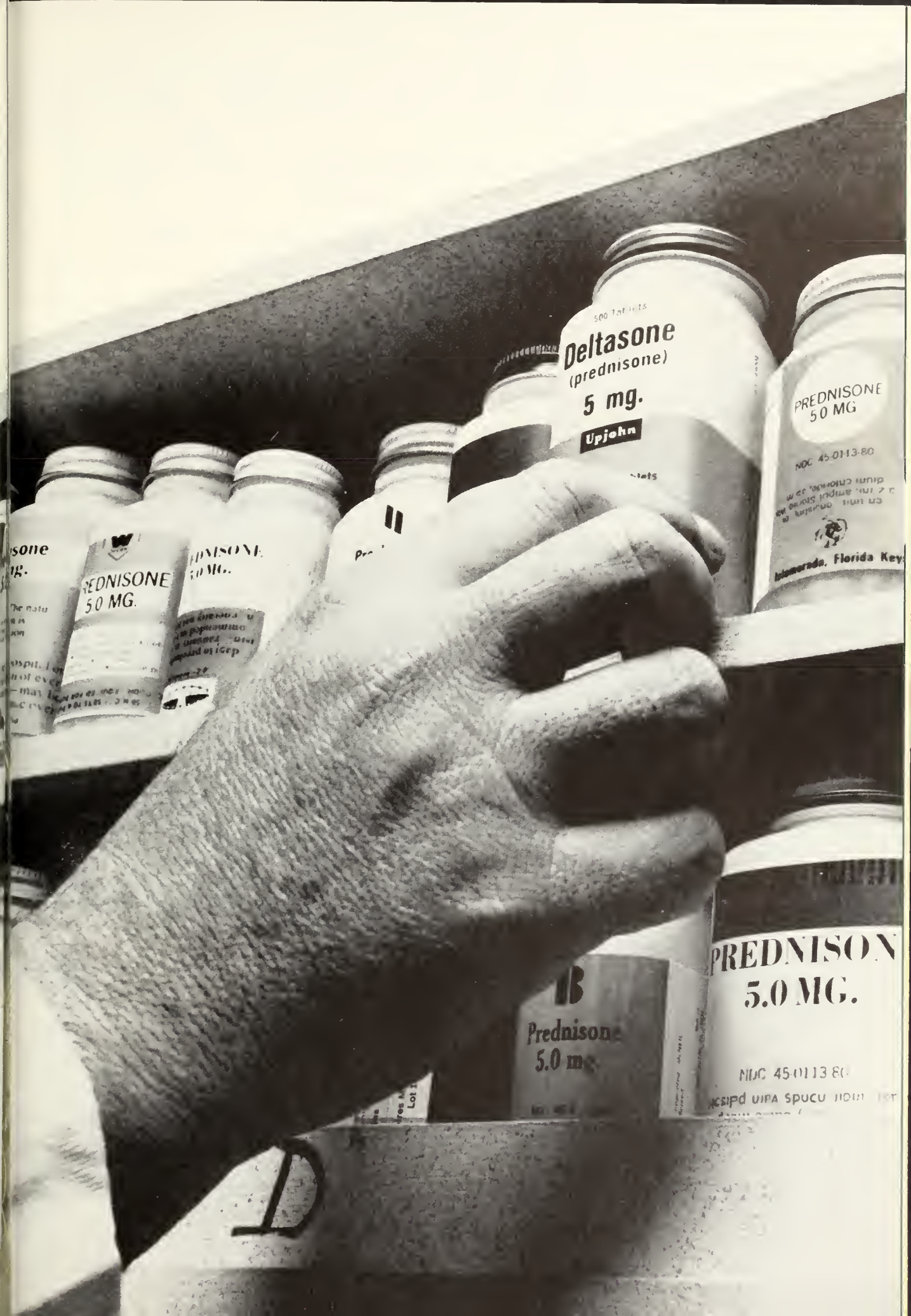
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Contraindications: As for all other corticoids. *Considered Absolute*—herpes simplex keratitis, acute psychoses and latent, healed or active tuberculosis. May be lifesaving in certain cases of pulmonary or meningeal tuberculosis, but should be used only in conjunction with adequate and effective antituberculous therapy to which causative organisms are shown to be sensitive. *Considered Relative*—active or latent peptic ulcer, Cushing's syndrome, diverticulitis, fresh intestinal anastomoses, osteoporosis, renal insufficiency, thromboembolic tendencies, psychotic tendencies, diabetes mellitus, hypertension, local or systemic infections including vaccinia, varicella and other exanthematous diseases, and fungal infections, and, pregnancy particularly during the first trimester because of observation of fetal anomalies in experimental animals. If necessary to give corticosteroids during pregnancy, watch newborn infants closely for signs of hypoadrenalism and institute appropriate therapy if signs appear.

If corticoids are used in the above conditions, weigh risks against benefits.

Precautions: Deltasone should be given only with full knowledge of characteristic activity of and varied responses to corticoids. Because of inhibiting effect on fibroplasia, corticoids may mask signs of and enhance spread of infection; hence, watch patients closely, and if intercurrent infection occurs, control with appropriate antibacterial measures. If possible, avoid abrupt cessation of corticosteroid therapy because of the danger of superimposing adrenocorticoid insufficiency on the infectious process. Prolonged hormone therapy usually causes a reduction in the activity and size of the adrenal cortex. When discontinuing therapy, relative adrenocortical insufficiency may be avoided by gradual reduction of dose. However, a potentially critical degree of insufficiency may persist asymptomatically for some time even after gradual discontinuation of adrenocortical steroids. Therefore, if a patient is subjected to significant stress, such as surgery, trauma, or severe illness while being treated, or within one year (occasionally up to two years) after treatment has been terminated, hormone therapy should be augmented or reinstituted and continued for the duration of the stress and immediately following it. Since mineralocorticoid secretion may be impaired, salt and/or desoxycorticosterone should be administered conjunctively. It is preferable to use a soluble hormone preparation in the immediate preoperative and postoperative periods.

Although unlikely with Deltasone, average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium and calcium excretion. Dietary salt restriction and potassium supplementation may be necessary. Glucocorticoid steroids may aggravate diabetes mellitus so that higher insulin dosage may become necessary or manifestations of latent diabetes mellitus may be precipitated. Corticosteroids may aggravate myasthenic symptoms in myasthenia gravis and should be given with proper precautions.

Muscle weakness, in some instances, attributed to hypopotassemia, has been reported following prolonged systemically administered corticoids. Excessive potassium loss, like excessive sodium retention, is not likely to be induced with effective maintenance doses of Deltasone (prednisone), however, keep this eff in mind and perform periodic serum potassium determinations patients on prolonged corticoid therapy. Muscle weakness occ ring with normal serum potassium levels may be due to disturban in muscle metabolism. Severe myopathy is associated with su stantial doses of steroids for prolonged periods, and eviden indicates it occurs more frequently with 9-alpha-fluro steroids. F placement with non-fluorinated steroid has, in some instances, sulted in improvement.

Retardation of linear growth, roughly proportional to dose, h been noted in children on corticoids for six months or more. Follo ing cessation of therapy, growth rate may be accelerated. Ther fore, carefully observe growth of children on prolonged cortic and if growth is retarded, reduce dose sufficiently to permit recove before epiphyseal closure. Make every effort to avoid corticoi during pregnancy, since spontaneous remission of some diseas such as rheumatoid arthritis may occur. Long term corticoid thera may evoke hyperacidity or peptic ulcer, therefore, as prophylax an ulcer regimen and antacid are highly recommended. Take X-ra in peptic ulcer patients complaining of gastric distress, an whether or not changes are noted, an ulcer regimen is recor mended. Since prednisone causes less salt and water retentic than many other glucocorticoids, patients should be observe closely for development of undesirable hormonal effects that a less obvious indications of steroid toxicity than edema and hype tension due to salt and water retention. Continued supervision patients after cessation of therapy is essential, since there may b a sudden reappearance of severe disease manifestation.

Adverse Reactions: Adverse reactions associated with use of cor coids include: Cushing's syndrome, moon facies, supraclavicul fat pads, hirsutism, striae and acne; relative adrenocortical insuff ciency particularly in time of stress due to trauma, surgery severe illness; protein catabolism with negative nitrogen balanc electrolyte imbalance; alteration of glucose metabolism with aggr vation of diabetes mellitus including hyperglycemia and glycosuri osteoporosis reversible only with difficulty; spontaneous fracture aseptic necrosis of the hip and humerus; activation and complic tion of peptic ulcer including perforation and hemorrhage; aggr vation or masking of infection; increased blood pressur convulsions; petechiae and purpura; menstrual irregularities i cluding amenorrhea, spotting or prolonged bleeding; insomni psychic disturbances especially abnormal euphoria; nervousnes posterior subcapsular cataracts occasionally requiring extractio increased intraocular tension; increased intracranial pressure wi papilledema (pseudotumor cerebri); pancreatitis; necrotizing ang itis; thinning of scalp hair; suppression of growth in childre thromboembolic complications; facial erythema; allergic skin rea tions; ulcerative esophagitis; sweating; vertigo; weakness; myop athy; headache; exophthalmos. Adverse reactions are usual reversible and usually disappear when drug is discontinued.

Supplied: 2.5 mg., scored—bottles of 100 tablets. 5 mg., scored bottles of 100 and 500 tablets and cartons of 100 tablets in fo strips.

For additional product information, consult the package inse or see your Upjohn representative.

MED B-1S (KQB-

Upjohn The Upjohn Company, Kalamazoo, Michigan 49001

Deltasone® 5 mg. (prednisone, Upjohn)

an economical prednisone that's made a name for itself

The concert was just underway,
When to the conductor's dismay
Cramps and diarrhea,
Did so quickly appear,
The maestro no longer could stay.

Because diarrhea with cramping, nausea, and painful straining can strike at the most inopportune time, it takes a comprehensive agent to treat the total diarrheal syndrome and help get the patient back on the job. That's why so many physicians rely on Donnagel, especially during the fall and winter months when "flu" and viral gastroenteritis usually hit their peak.

Donnagel is much more than just a simple kaolin-pectin combination. It also contains the belladonna alkaloids to calm GI hypermotility and help relieve the distressing discomforts which so often accompany diarrhea. Certainly it's less expensive and more convenient than taking two medications. And the dosage is lower too. Available in the handy 4-oz. plastic bottle at pharmacies everywhere on your prescription or recommendation.

When diarrhea and its discomforts separate a man from his job . . .

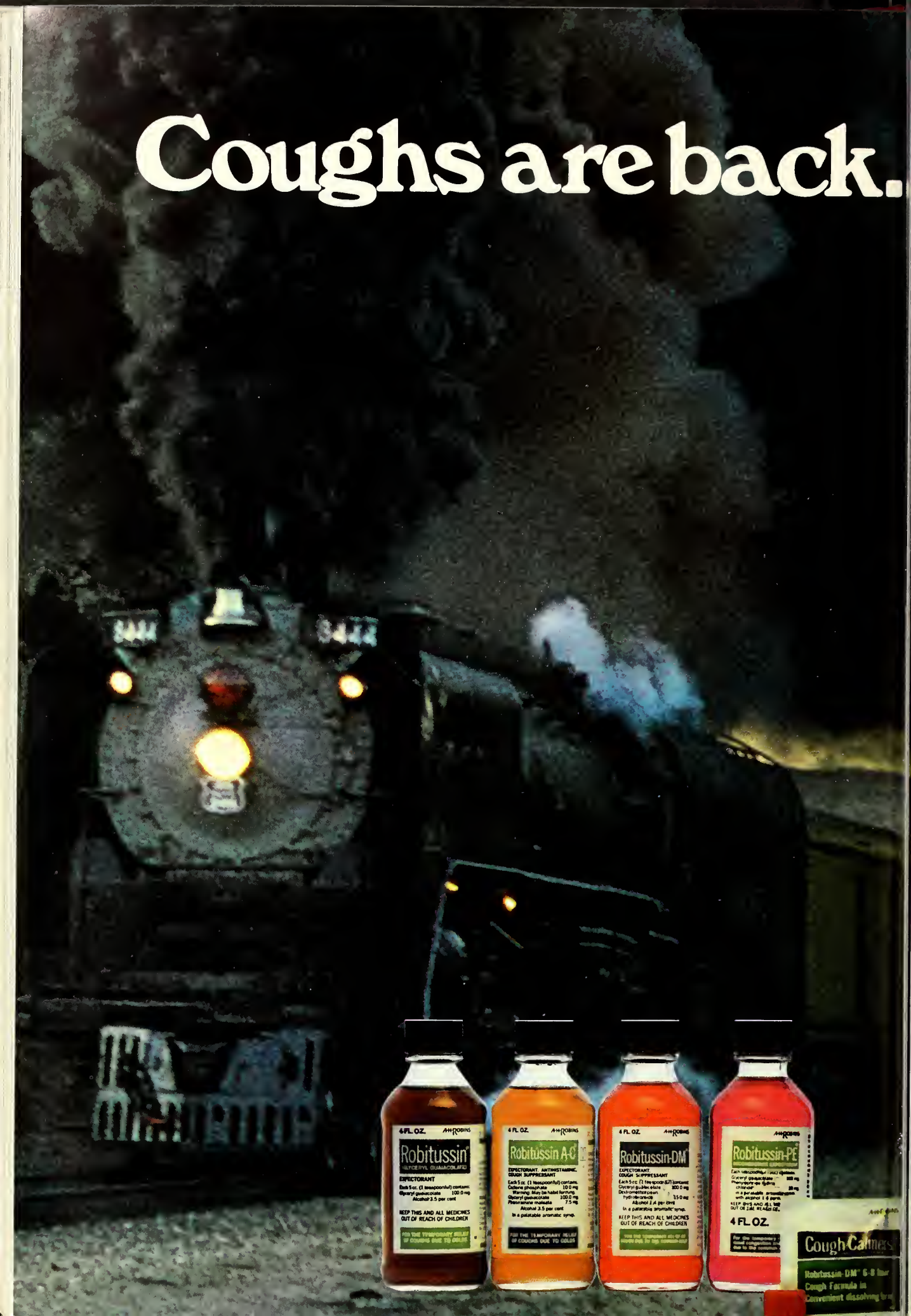
Donnagel®

Each fluid ounce contains: Kaolin, 6 g.; Pectin, 142.8 mg.; Hyoscyamine sulfate, 0.1037 mg.; Atropine sulfate, 0.0194 mg.; Hyoscine hydrobromide, 0.0065 mg.; Sodium benzoate (preservative), 60 mg.; Alcohol, 3.8%.

A·H·ROBINS

A. H. Robins Company,
1407 Cummings Drive,
Richmond, Va. 23220

Coughs are back.



clear the tract with the

Robitussin® Line

The coughing season is here again. Time to rely on the four Robitussins and Cough Calmers to help clear the lower respiratory tract. All contain glyceryl guaiacolate, the efficient expectorant that works systemically to help increase the output of lower respiratory tract fluid. The enhanced flow of less viscid secretions soothes the tracheobronchial mucosa, promotes ciliary action, and makes thick, inspissated mucus less viscid and easier to raise. Available on your prescription or recommendation.

For coughs of colds and "flu"

Robitussin®

Each 5 cc. contains:

Glyceryl guaiacolate	100.0 mg.
Alcohol, 3.5%	

For unproductive allergic coughs

Robitussin A-C®

Each 5 cc. contains:

Glyceryl guaiacolate	100.0 mg.
Pheniramine maleate	7.5 mg.
Codeine phosphate	10.0 mg.
(warning: may be habit forming)	
Alcohol, 3.5%	

Non-narcotic for 6-8 hr. cough control

Robitussin-DM®

Each 5 cc. contains:

Glyceryl guaiacolate	100.0 mg.
Dextromethorphan hydrobromide	15.0 mg.
Alcohol, 1.4%	

Clears sinuses and nasal stuffiness as it relieves cough

Robitussin-PE®

Each 5 cc. contains:

Glyceryl guaiacolate	100.0 mg.
Phenylephrine hydrochloride	10.0 mg.
Alcohol, 1.4%	

Robitussin-DM in solid form for "coughs on the go"

Cough Calmers™

Each Cough Calmer contains:

Glyceryl guaiacolate	50.0 mg.
Dextromethorphan hydrobromide	7.5 mg.

Select the Robitussin® "Clear-Tract" Formulation That Treats Your Patient's Individual Coughing Needs:

Robitussin® extra benefit chart

All 5 Robitussins have an EXPECTORANT-DEMULCENT action. Keep this handy chart as a guide in selecting the formula that provides the *extra* benefits you want for your patient.

	Cough Suppressant	Antihistamine	Long-Acting (6-8 hours)	Nasal, Sinus Decongestant	Non-Narcotic
ROBITUSSIN®					●
ROBITUSSIN A-C®	●	●			
ROBITUSSIN-DM®	●		●		●
ROBITUSSIN-PE®				●	●
COUGH CALMERS™	AHR		AHR		AHR

A. H. Robins Company, Richmond, Va. 23220 A·H·ROBINS

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TELEPHONE
774-8276 FOR

Insurance for Members

OFFICIALLY ENDORSED by the

MAINE MEDICAL ASSOCIATION

DOW & PINKHAM

107 EXCHANGE STREET, PORTLAND

This contract provides physicians' services and benefits to the extent herein defined and limited.

Blue Shield Plans

OF THE

Associated Hospital Service of Maine

(Herein Called A. H. S.)

PORTLAND, MAINE

Certificate of Coverage for Physicians' Service Benefits

This is to Certify: That the Subscriber and Family Members, if any, named on the Subscriber's Identification Card issued as a part of this Contract, are entitled to benefits in accordance with the terms, conditions and provisions appearing hereinafter and made a part hereof.

In Witness Whereof Associated Hospital Service of Maine (a Non-profit Maine Corporation) has duly executed this Contract.

Countersigned by:

President

Chairman of the Board

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Blue Shield Office/OPD/ Home Benefits Can Prevent Unnecessary Admissions

We remind you that the following services are covered by Blue Shield when performed *by a physician in private practice* in the physician's office, the patient's home, or the outpatient department of the hospital:

- Emergency care within 72 hours of an accident
- Surgical and fracture procedures

The following diagnostic procedures (except as part of a routine physical):

- X-rays (other than teeth)
- EKG's
- EEG's
- Protein bound iodine tests
- Radioactive iodine uptake tests
- T-3 tests
- T-4 tests
- Basal metabolism tests
- Lab examinations of spinal fluid and surgically removed tissue

PUBLISHED TO REPLACE A PREVIOUS ADVERTISEMENT WHICH THE FOOD AND DRUG ADMINISTRATION CONSIDERED MISLEADING

The Food and Drug Administration has requested that we bring to your attention a recent promotional campaign for Garamycin Injectable (gentamicin sulfate) which featured a nationwide *in-vitro* hospital survey involving a comparison of sensitivity patterns of Garamycin Injectable and seven other antibiotics.

The FDA considers the advertising misleading in several respects such as:

The *in-vitro* chart contained in the ads, which compared Garamycin Injectable with seven other antibiotics, implied that Garamycin Injectable is clinically more effective than the seven other compared antibiotics. THE FACTS ARE (1) THAT DIRECT EXTRAPOLATION OF NONCLINICAL FINDINGS TO CLINICAL EFFECTIVENESS IS UNWARRANTED, AND (2) THAT THE ADVERTISED *IN-VITRO* COMPARISONS DO NOT CONSTITUTE A VALID BASIS FOR SUGGESTING THAT GARAMYCIN INJECTABLE HAS GREATER CLINICAL EFFECTIVENESS THAN THE COMPARED ANTIBIOTICS.

The *in-vitro* chart and information contained under the ad heading, "Indications" presented *in-vitro* data results in such a way as to imply that the drug is indicated for Gram-positive bacteria, such as *Staphylococcus aureus*. GARAMYCIN INJECTABLE IS NOT APPROVED FOR INFECTIONS DUE TO ANY GRAM-POSITIVE ORGANISMS.

We emphasize that Garamycin Injectable is approved for use only in infections due to susceptible strains of gram-negative bacteria, including Pseudomonas aeruginosa, and species of indole-positive and indole-negative Proteus, Escherichia coli, and Klebsiella-Aerobacter.

Injectable Garamycin®

brand of gentamicin sulfate injection

Schering

Each cc. contains gentamicin sulfate equivalent to 40 mg. gentamicin

BRIEF SUMMARY

INDICATIONS GARAMYCIN Injectable is clinically effective in infections due to susceptible strains of gram-negative bacteria, including Pseudomonas aeruginosa, and species of indole-positive and indole-negative Proteus, Escherichia coli, and Klebsiella-Aerobacter. Bacteriologic studies should be conducted to identify the causative organism and to determine its sensitivity to gentamicin sulfate. Sensitivity discs of the drug are available for this purpose. If the susceptibility tests indicate that the causative organism is resistant to gentamicin sulfate, other appropriate antibiotic therapy should be instituted.

This drug should be limited to the treatment of serious infections caused by gram-negative bacteria, particularly Pseudomonas aeruginosa, Proteus and other susceptible organisms, with due regard for relative antibiotic toxicity. Therefore, the drug should be considered for use against gram-negative: 1. Bacteremia; 2. Infected surgical wounds; 3. Severe soft tissue infections, including burns complicated by sepsis; 4. Respiratory tract infections; and 5. Selected cases of urinary tract infection.

CONTRAINDICATIONS GARAMYCIN Injectable is contraindicated in individuals with a history of hypersensitivity or toxic reactions to gentamicin.

WARNINGS Patients receiving treatment with GARAMYCIN should be under close clinical observation because of the toxicity associated with the use of this drug. Ototoxicity, vestibular and auditory, can occur in patients, primarily those with pre-existing renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with pre-existing renal impairment. Kidney function diminished by infection of the upper urinary tract may, however, improve during effective treatment with GARAMYCIN Injectable.

Concurrent administration of potentially ototoxic drugs such as streptomycin and kanamycin or of potentially nephrotoxic drugs such as polymyxin, colistin, and kanamycin with gentamicin sulfate has not been shown to afford any clinical advantages and, moreover may result in additive toxicity. Monitoring of vestibular, cochlear, and renal function will provide guidance for therapy in such cases.

PRECAUTIONS In patients with impaired renal function in whom serious infection develops, serum concentrations of the drug may rise, with consequently increased risk of ototoxicity. In these patients or in those in whom recommended dosage or duration of therapy must be exceeded as a life-saving measure, routine studies of kidney function should be performed when possible. These may be supplemented by evaluation of the vestibular and auditory function and measurement of serum concentration of the drug when feasible. Serum concentration of gentamicin should be maintained below the range of 10-12 mcg./ml. to reduce risk of ototoxicity.

Ordinarily, treatment should not be given for more than 7 to 10 days or be repeated unless required for serious infection not responsive to other agents.

As with other antibiotics, treatment with GARAMYCIN Injectable may occasionally result in overgrowth of nonsensitive organisms. If superinfection occurs, appropriate therapy is indicated.

Safety for use in pregnancy or the potential for fetal ototoxicity or nephrotoxicity have not been established. Studies in pregnant animals have not revealed teratogenic or ototoxic effects in the fetus. GARAMYCIN Injectable should not be used in pregnant patients or in women of childbearing age unless its use is deemed advisable by the physician.

ADVERSE REACTIONS The overall incidence of ototoxicity considered related to treatment with GARAMYCIN Injectable was 2.8 per cent (16 of 565 patients). Contributory factors (two or more factors were relevant to most patients) were as follows: 10 had azotemia, 10 received a total of 1 gram or more of the drug, 7 had recently received other potentially ototoxic antibiotics (streptomycin or kanamycin), and 5 were over 60 years of age. Six also had decreased high-tone hearing acuity, which returned to or toward normal in the 4 patients retested.

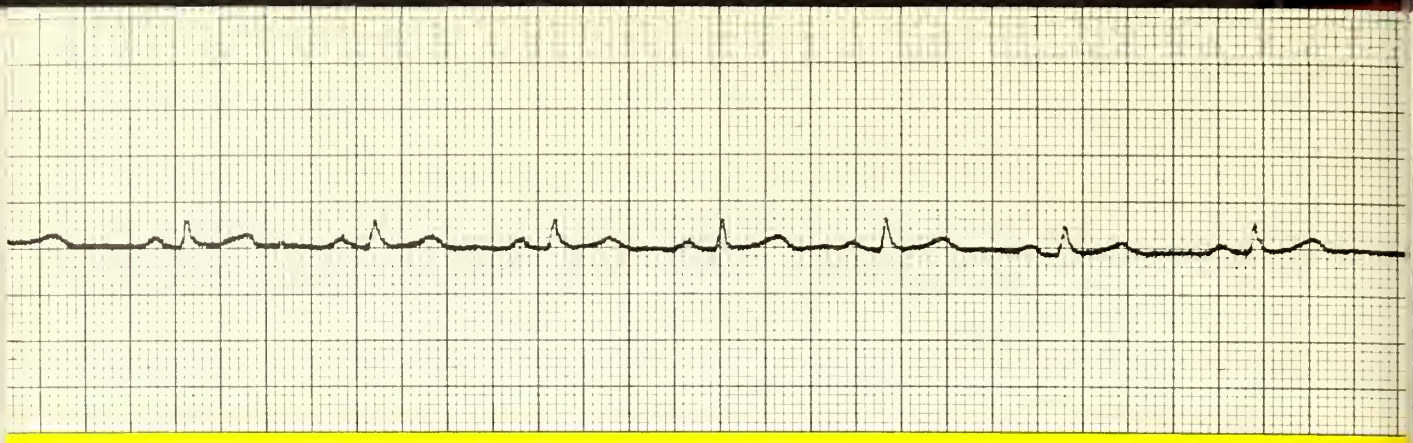
Analysis of BUN data indicated that 4 (2%) of 172 patients showed increases in BUN that were probably related to treatment with GARAMYCIN Injectable. Of 20 increases probably or possibly related to treatment, 7 were reversible, 9 occurred in terminal patients, and 4 had no follow-up.

Other adverse reactions associated with treatment were one instance each of urticaria, decreased hematocrit, and reversible depression of granulocytes with normal bone marrow. Other rarely reported and possibly treatment-related adverse reactions were anemia, increased reticulocyte count, rash, purpura, drug fever, hypotension, convulsions, twitching, salivation, nausea, vomiting, increased transaminase activity (SGOT or SGPT), increased serum bilirubin, decreased serum calcium, and joint pain.

PACKAGING GARAMYCIN Injectable, 40 mg./cc., 2-cc. multiple-dose vials, for intramuscular administration.

SCHERING CORPORATION, UNION, NEW JERSEY 07083

SCH-2620



When disease is ruled out and psychic tension is implicated

Valium® (diazepam)

helps relax the patient and relieve his somatic symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms have occurred following abrupt discontinuance. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation, have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

ROCHE

Roche
LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110